A

TREATISE ON HÆMOP

DR WICKHAM LEG

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SOMETIMES CALLED THE

HEREDITARY HÆMORRHAGIC DIATHESIS

BY

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Omnia membra
Emisere simul rutilatum sanguine virus:
Sanguis erant lacrimae: quaecumque foramina novit
Humor, ab his largus manat cruor: ora redundant
Et patulae nares: sudor rubet: omnia plenis
Membra fluunt venis; totum est pro vulnere corpus.

LUCANI *Pharsalia.*

LONDON

H. K. LEWIS 136 GOWER STREET

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PREFACE

The following pages have been written for some time past: they were at first designed to form part of a larger work; but they are now published separately, as there exists no complete account of hæmophilia in the English language.

My attention was first drawn to this disease, nearly nine years ago, by seeing a boy, the subject of hæmophilia, bleed to death of a simple epistaxis: since that time I have made careful study of almost every case that has fallen under my observation; and have endeavoured, so far as my opportunities extended, to make myself acquainted with whatever has been written on this subject.

I have not attempted any new statistical observations: firstly, because all deductions drawn from statistics based upon observations which have been contributed by different writers, are liable to grave error; and secondly, because the time seemed too

short, that has gone by since Lange published his careful researches, supplemented as they have been by those of Grandidier in 1863, for much information to be gained by a new collection of figures.

LONDON *January 1st*, 1872.

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ERRATUM.

While the sixth chapter of this work was passing through the press, I received from Germany Schliemann's Würzburg dissertation, *De dispositione ad haemorrhagias perniciosas haereditaria.* It was immediately apparent that the case, that I have quoted at p. 83 from Grandidier, as the report of Schliemann's *post mortem* examination of a Jew boy suffering from hæmophilia, is altogether worthless: from the clinical history of this patient, which is given at p. 11 of the dissertation, it is plain, to the most careless reader, that the patient, whose examination after death is recorded, was suffering from purpura, or the *morbus maculosus Werlhofii*, as Schliemann himself remarks, and not from hæmophilia of any degree.

ADDENDUM.

At the moment at which this work is published, an important observation has appeared in *Lyon médical* for Dec. 24, 1871, on the *post mortem* examination of the joints in hæmophilia; I can now do no more than point out to the student the existence of a great addition to our knowledge of the morbid anatomy of the joint swelling.

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CHAPTER I.

INTRODUCTORY.

BY Hæmophilia is meant a disease, both hereditary and congenital; usually lasting throughout the life of the patient; accompanied by a hæmorrhagic diathesis, and a tendency to swelling of the joints. CHAP. I.

The liability to abundant and long-continued bleedings is one of the chief symptoms of hæmophilia. But the hæmorrhages must not merely be obstinate and prolonged; the tendency to bleed must be congenital, or almost congenital. It must not be assumed that every case, in which it is difficult to stop the flow of blood, is one of hæmophilia. A tendency to great hæmorrhage sometimes appears in the course of certain diseases, and may even last for years: but hæmophilia is a disease which shows itself in infancy, and persists, as a rule, throughout the life of the patient.

In England this disease is often called the hæmorrhagic diathesis, or tendency. I have preferred to use the name hæmophilia, because hæmorrhagic diathesis has too wide a meaning. It would include all diseases in which a hæmorrhagic tendency is present; and it is also wanting in definition since it does not connote

CHAP. I. the hereditary and congenital character of the disease, nor the tendency to swelling of the joints; this swelling of the joints is often a more marked feature in the disease than the bleeding. The tendency to hæmorrhage is only one symptom of this constitutional disorder.

On the continent, the disease is universally called hæmophilia,[1] or hæmorrhaphilia.[2] The former of these names is the more commonly used; neither is good, but it is now too late to attempt to change. In Germany hæmophilia is also called *Bluterkrankheit;* less commonly *Blutsucht* or *Blutungssucht;* and individual patients, *Bluter*, a translation of the word *bleeder*, used

[1] The etymology of the word seems to be plain: αἷμα and φιλία. M. de Fleury, however, prefers to derive the name from φυλή, a race, or tribe; with reference, I suppose, to its hereditary character (*Mém. de la Soc. méd.-chir. de Bordeaux*, t. i., p. 303.) This derivation necessitates a change in the accustomed manner of spelling: but all the early German authors write the word *hämophilie*: to which I have therefore adhered.

Various other names have been proposed: hæmorrhophilia, hæmatophilia, hæmorrhagophilia, idiosyncrasia hæmorrhagica, and morbus hæmaticus. A name proposed by Uhde (*Deutsche Klinik*, 1850, p. 539), is amychæmorrhagia, from ἀμυχή, a slight wound: perhaps it is the worst yet suggested.

[2] Hæmorrhaphilia is the name used by Schönlein in his *Vorlesungen* (third edit., 1837.) Virchow (*Handb. d. spec. Path. und Ther.* i. 264,) seems to think that Schönlein was the author of the word hæmophilia. I am unable to say from my own observation by what writer the name was first used. *Die Hämophilie* is said to be the title of an inaugural dissertation by Hopf, at Würzburg, in 1828. The word is so barbarous and senseless that it is not wonderful that no one should be proud of it.

by the American physicians[1] who first described cases of this disease. In France the disease is now always called *hémophilie*. In the older books it is called *diathèse hémorrhagique*, *hémorrhaghie constitutionnelle*, *purpura constitutionnel*. The patients are called *hommes saignants*, but more commonly the German *Bluter* is used.

The notes of a few cases of hæmophilia which have fallen recently under my own observation are here given: the first four cases have been already published.[2] All the patients were natives of London.

Richard Bickell, born April 28, 1859, was brought to Saint Bartholomew's Hospital on April 27, 1871.

The following history was given by his maternal grandmother.

His father is alive, aged 35; by occupation a paper-hanger; he was born in Devonshire. He is not subject to bleedings, nor are any of his brothers or other relations, to the best of informant's knowledge; they do not suffer from gout. This man enjoys good health, but is very subject to catarrhs. He was no relation to his wife.

His mother had always weak health; she was not subject to excessive floodings or menstruation. She died when 29 years old. She had been delivered of her fourth child about a month, and was sitting in an easy

[1] Otto, *Medical Repository*, New York, 1803, vol. vi. p. 3.
Hay, *New England Journal of Medicine and Surgery*, Boston, 1813, vol. ii. p. 223.

[2] In the *Saint Bartholomew's Hospital Reports*, 1871, vol. vii. p. 23.

CHAP. I. chair, apparently very well, in the same room with informant, when she suddenly called out: Mother, it is dark; she fell back, and was dead in a few minutes: during all her life she had had a beating at the heart, and the last few years she was subject to a cough in the winter. She was an only child; she married when 20 years of age, and had four children:

Richard, the present patient, a bleeder.

Girl, aged 10, not a bleeder; she enjoys good health.

Girl, aged 8, not a bleeder; she enjoys good health, but this summer has been subject to bleedings from the nose.

Boy, aged 6; he bleeds often at the nose; and when the bleeding comes on it lasts three or four days. When he is bruised, there are seen large black and blue patches under his skin; but no spontaneous ecchymoses have been noticed. He was vaccinated when he was three months old, and the bleeding was not more than is ŭsual with other children. The vesicle ran its usual course. All these children were born in London.

My informant says that she knows none of her own relations to be subject to bleedings. Her husband is subject to a cough and symptoms of dyspepsia, but not to bleedings or gout. She herself is 55 years old, very stout. All her life she has been subject to 'gravel in the kidneys,' and says she has passed several small stones with the urine.

The patient was born at the full time; there was no difficulty in stopping the bleeding after the cutting of the navel string, nor any bleeding when the stump fell off. The boy was vaccinated when three months old, there was no unusual bleeding, the inoculation being

successful. The mother suckled him herself for twelve months.

When the teeth of the first dentition came through, there was no unusual bleeding. But these teeth decayed early; and when he was between 4 and 5 years old, one of the back teeth was taken out for this reason. The bleeding from the socket lasted three weeks, and defied every styptic. An attempt was made to use the hot iron, but was abandoned from the restlessness of the child. The boy was quite bloodless when the bleeding came to an end of itself. This was the first hæmorrhage of any kind noticed.

When he was 6 years old, his left knee began to swell, and this joint has been swollen, off and on, ever since. The knee may keep well for three or four months; it then begins to swell, and will be painful and large for several months at a time, so that the boy is seldom free from trouble with his joints. Sometimes, as the swelling is disappearing in the left knee, it appears in the right, and *vice versâ*. Sometimes the ankles swell; but the left knee is the joint most commonly disabled. No swelling has been noticed in any other joints. No difference has been noticed in summer or winter, or in cold or wet weather.

He was 3 years old when he had the measles; and was 5 years old when he had the whooping-cough, after which he was six weeks in the Hospital for Sick Children. He has never had scarlet fever, small-pox, or any other disorder.

Three months ago a tooth gradually became loose, and though great care was taken that it should not be pulled out, yet one night, when it was attached by a

 mere thread to the gum, it came away; the bleeding then lasted a week, defying such styptics as alum and gallic acid; after ceasing for a few hours, it began again, and lasted another week, making a fortnight altogether. He has never been subject to epistaxis or hæmaturia, nor to any other spontaneous hæmorrhages. When blisters are applied, as, for example, to the knee, no ill effects follow.

The boy's schoolmaster tells my informant that he is 'first class at his book.' The boy himself says he is glad to go to school, and he seems intelligent for his age.

The boy has brown hair, blue eyes, and a thin skin. The cheeks and eyes are sunken, he looks thin and pale, and has a worn aspect, such as those have who have suffered much pain. The chief trouble is his knee: two nights ago it was swollen as big as his head; but the next morning it had very greatly diminished. There is now a swelling which fluctuates very plainly, and upon which the patella floats. The right ankle is also swollen, but not very greatly: neither joint is painful. There is nothing unnatural about the heart.

The knee was strapped; and the grandmother was told to give him a teaspoonful of cod liver oil and steel wine three times a day.

May 11.—The boy has remained under observation until the present time. He is now shedding his back milk teeth, and there is a constant oozing of blood going on from the gums.

James Cameron, aged 24, first came under my notice in October 1868. He was born in Clerkenwell, and was

a sailor by occupation, going in steam and sailing ships to Australia, Constantinople, &c. He was a man of middle stature, fair hair, and light gray eyes. There was a complete absence of whiskers and only a slight moustache; but abundance of hair over the pubes. The skin was thin. The intelligence was somewhat below the average. He was suffering from erysipelas of the head and face; and in consequence of this a collection of matter formed under the skin of the neck, just below the parotid gland. On October 17, the abscess was opened by a small incision, which bled, at the most, but a few drops; pus escaped, and the neck was poulticed. On the 19th a sinus had formed which admitted a probe for two inches; the skin was then cut through on to the point of the probe, and a few threads passed through the sinus to assist the drainage: some slight venous hæmorrhage followed. He went on well till October 23, when the bottom of the sinus began to bleed: iced water and plugging were of no avail; indeed, the plugging caused such a sensation of choking that the lint had to be taken out. On October 25, the skin over the sinus having sloughed, it was divided, and all the coagula turned out. Thereupon the bleeding ceased. On October 28 there was again slight bleeding, and on October 30 the wound was granulating.

He now stated that he had been subject all his life to bleedings upon slight accidents; that he had often been in hospital for the bleedings from small wounds, difficult to stop; and that, if he had a tooth drawn, the bleeding lasted for days. He had never suffered from swellings of the joints.

The mother of the patient gave me the following

CHAP. I. story. She herself, aged 64, enjoyed good health, and was not a bleeder, but her father was, and he was the first bleeder in her family of whom she knows. This man married a wife to whom he was no relation, and had by her a numerous family of sons and daughters, only two of whom reached maturity. My informant did not know the causes of the deaths of her brothers and sisters, or whether they were bleeders. Of the two children who grew up one was my informant, and the other, a man, not a bleeder, died aged 64, of 'cancer of the tongue.' He had no children.

My informant was twice married: in neither case was her husband any relation. In all she had twelve children:

By first marriage:

1. Boy, not a bleeder, died, aged 40, of poison.

2. Boy, not a bleeder, died, aged 5, of small-pox.

By second marriage:

1. Boy, alive, age not exactly known, but over 35, is not a bleeder.

2. Boy, died, aged 3, of whooping cough, not a bleeder.

3. Boy, alive, aged 32, not a bleeder.

4. Boy, died, aged 6, of 'typhus fever,' not a bleeder.

5. Boy, alive, aged 29, a bleeder. This was first noticed when he was eighteen months old; he had a fall, bit his tongue, and bled furiously. The mother says he is a 'frightful bleeder;' if he has a tooth loose or a cut made, he bleeds 'awfully.'

6. Boy, died, aged 25, of dropsy and diseased heart following rheumatic fever. He was a bleeder. The mother believes he used to have the gout, for he had

'chalk stones up the sides of his feet.' Hard masses could be felt under the skin, but they did not come through. He was six years old when he had the rheumatic fever, and was seven years of age when the diseased heart was first recognised.

7. Boy, died when three or four years old of scarlet fever; a bleeder.

8. Miscarried at six months of a male fœtus.

9. Is patient, aged 24. He was first noticed to be a bleeder when he began to shed his milk teeth at six years old.

10. Girl, died at four years of age of 'typhus fever;' not a bleeder.

The patient's father is 68 years old; he enjoys good health, and is not a bleeder, nor are any of the paternal relations; but both the father and his relations are gouty. The father had only one brother who died gouty; and who had only two children, both of whom died idiots in lunatic asylums.

My informant has only one grandchild, aged 9 months; no signs of bleeding have appeared (October, 1868.)

Cameron was alive and well in April 1871; but his mother died in the autumn of 1869.

James Day, aged 8 years, was brought by his mother to Saint Bartholomew's Hospital on April 10, 1871, suffering from repeated bleedings from his mouth. His mother gave the following account of his family.

The father is alive, aged 30; he was born in Whitechapel, and enjoys good health. By occupation he is

CHAP. I. a porter; he is not subject to bleedings nor to the gout. He has had two brothers, both older than himself; one aged 40, is subject to bleedings; when he has a tooth drawn, or wounds himself, a bleeding follows which is difficult to stop. This man has seven children, three boys and four girls, who are not subject to bleedings. The other brother was also subject to excessive bleedings upon slight causes; he was killed, age unknown, while following his trade as an armoury sergeant, by the explosion of some weapon. The father had only one sister, who died, aged 30, of consumption. She had only two children, both girls; they are not subject to bleedings.

The mother, aged 30, looks in good health; her menstruation has always been regular and not excessive. She has only once been pregnant. She has two brothers, but they do not suffer from bleedings; none of her relations are subject to bleedings to her knowledge. She is no relation to her husband.

The boy was born in Bethnal Green, at full time; the mother does not remember any difficulty with regard to the falling off of the navel string; he was suckled till fifteen months old. When sixteen months old he was vaccinated, and the incisions were unattended by any unusual bleeding, and the vesicles ran their usual course. When two years old he had the measles, and the mother thinks he has never been well since. He has had no other disease of childhood, as whooping-cough, scarlet fever, or small-pox. He has lived in London all his life.

The mother has never noticed any black or blue spots on the skin; nor when he is bruised do the parts be-

come much ecchymosed. He is not subject to pains in the limbs or swellings of the joints. CHAP. I.

The tendency to bleeding was first noticed when the boy was five years old; it then showed itself by repeated attacks of epistaxis which lasted for a quarter of an hour or more; these were always more severe in the summer than in the winter, and then came on as well by day as by night. The bleeding occurred several times in a week. But for the last four months the bleeding from the nose has ceased, and the bleeding now comes from the mouth, but she has not noticed from what part. This bleeding only comes on at night; yet the mother says it happens every night.

The boy has no unusual bleeding when a tooth is taken out or when he cuts his finger.

He has very light coarse hair and gray eyes; the skin is perhaps a little delicate, but the veins are not prominent. Nothing unnatural can be seen in the mouth; the first sound of the heart at the base is not healthy. The mother complains that he reads two much, and boy is certainly more intelligent than those of his class and age are wont to be. He is thin, but his appetite is good. He is chilly, and complains much of the cold. He was told to take a teaspoonful of cod liver oil and steel wine three times a day.

The patient still remains under observation (October, 1871); the general health greatly improved, and the bleedings have disappeared for two months. The tincture of the perchloride of iron in 10 minim doses seems to have had the best result as an astringent.

James Hicks, born April 28, 1851, applied at Saint

CHAP. I. Bartholomew's Hospital on April 26, 1871, for the relief of bleeding from the nose.

He said that his father was alive, 45 years old, that he enjoyed good health, with the exception of frequent bleedings from the nose, which, however, are now easily stopped; when a young man he used to bleed 'just as I do,' after wounding himself, but a wound is not now followed by any extraordinary hæmorrhage. The patient has never heard of any of his father's relations being subject to bleedings, or to the gout, his father is not subject to the gout, nor is he any relation to his wife.

The mother is alive, aged 47; she enjoys good health, and is not subject to bleedings. The mother's brothers are not subject to bleedings. From this marriage there were seven children:

1. Present patient.

2. Boy, aged 18. He bleeds often from the nose, and the bleeding is difficult to stop when he is wounded.

3. Girl, died aged 18 months, of measles.

4. Boy, alive, aged 14. He has pretty good health, but the bleeding is considerable when he is wounded.

5. Boy, alive, aged 12. When wounded he bleeds much less than the others.

6. Boy, alive, aged 8. Now he has very good health; but he 'has been out of his mind, caused by a fright.' He bleeds very slightly when wounded.

7. Boy, died, aged 12 months, of 'fever.'

This patient was born in Bermondsey, and has lived in London all his life. He is a lighterman on the Thames. He says he has been subject to bleedings from the nose since his birth. He also says that he bruises very

readily; and that when he is wounded he bleeds so much that it is only stopped with great difficulty. Latterly, however, he has taken to putting tobacco on the wound, and he says that this stops the bleeding in five minutes. He points to a cut on the pulp of the finger, which was done five days ago, and which is now quite healed. He has never had a tooth drawn. He has never noticed any petechiæ, and has never passed blood in his water; occasionally there is a little blood in his spit, which he thinks comes from the gums. He is not subject to swellings of his joints; but he has great pains in the right knee, which are worse at night. Sometimes these pains are so great that he walks lame.

This man has light brown hair and gray eyes: he has no whiskers, but a slight moustache. There is a good deal of hair about the pubes. The skin is thick; the man's intelligence considerably below the average. The hands and feet are cold, and he says he feels the cold much. The bleedings from the nose have much increased during the past fortnight; they come on most at night, and in the early morning, and he has several times been obliged to plug the anterior nares with cotton.

Great improvement in the general health and considerable respite from the bleedings were obtained; twenty minims of the tincture of perchloride of iron were given three times a day with cod liver oil. In a month the bleeding from the nose had almost disappeared, while the pains in the keee were greatly diminished. He ceased shortly after to attend at the Hospital.

CHAP. I.

William Robins, aged 23, applied at Saint Bartholomew's Hospital on August 26, 1871, for the relief of swelling of the knee.

His father is alive, aged 47, subject to 'rheumatic gout' in all his joints for about 20 years; he has chalk-stones in his hands; and all his family are subject to the gout. He is not subject to bleedings; and he is no relation to his wife.

Mother alive, aged 40. She enjoys excellent health and is not subject to bleedings. She had only one brother, who was subject to bleedings from slight causes from his birth. When he was 20 years old, he met with some accident and broke his leg: it was cut off in one of the London Hospitals, the bleeding could not be stopped, and he died.

The patient's mother has borne six children:

1. Boy; present patient.
2. Boy, aged 21. He is not subject to bleedings, but enjoys excellent health.
3. Boy, died aged 7. He was subject to bleedings.
4. Boy, died a baby.
5. Girl, died aged 4. Cause unknown.
6. Girl, alive, aged 5. In good health.

The patient is a painter by trade; he is unmarried. There is a slight blue line round his gums.

He says he has been subject to bleeding since he can remember; his mother tells him that she first noticed this disposition when he was about 2 years old, from frequently-returning bleedings at the nose. When a child he used to bleed abundantly when he was pricked or scratched. The last time that he had any serious bleeding was about 3 years ago from a cut on the palmar surface

of the root of the left forefinger; the scar is less than half an inch long, and he says the wound was very slight; yet he was treated at Saint Bartholomew's for three weeks before the bleeding could be stopped. When he is struck, a large black and blue mark is nearly always left. Occasionally he notices similar black and blue spots on his arms and legs, without remembering a bruise or blow preceding them. Chap. I.

When the patient was about 4 years old, his mother first noticed a swelling of the right knee; this swelled, off and on, till the boy was 13 years old, and since that time it has never been of its natural shape and he has always walked lame. He has sometimes swellings of the ankles, but they only last a week at the most; once the joint between the proximal and middle phalanges of the right ring finger was swollen, but no other joints have been enlarged; he but occasionally feels pains in the hip and ankle. The knee joint is always worse in winter and upon changes of weather.

With the exception of the knee joint, he says that he enjoys pretty good health. Of the spontaneous hæmorrhages, epistaxis is his most frequent trouble: it is worse in the summer, and the nose may then bleed as often as two or three times in the day. But this summer the bleedings from the nose have been much less. His gums sometimes bleed, but he has never brought up any blood or passed blood by stool. He has only once had hæmaturia: this was last summer.

The man is of middle stature, muddy complexion, and dark brown hair; he has a good moustache and abundance of whiskers. The right knee joint is greatly crippled in its movements, it is also much enlarged on

the inner aspect and the swelling is very hard, as if the ends of the bones forming the joint were enlarged. The joint itself also seems to contain fluid.

His knee joint was strapped and he was given half a fluid drachm of the tincture of the perchloride of iron 3 times a day in water.

Sept. 2. He came back saying that he felt himself much better, both in health and as to the knee joint.

Nov. 1. 1871. The man has had no bleedings since he has been under treatment. The knee is not decreased in size.

CHAPTER II.

HISTORY OF HÆMOPHILIA.

THE history of a disease which has only recently become known must necessarily be short. There appears to be no notice of hæmophilia in the Greek or Latin authors. The earliest account of what seems like this disease is met with in the writings of Albucasis, an Arabic author who lived at Cordova in the 11th or 12th Christian century.[1] He relates that in a certain village there were men who when wounded, or phlebotomised, suffered an uncontrollable hæmorrhage, which ended only with the death of the patient. The same accident happened to the boys of the village if their gums were harshly rubbed; and hæmorrhage was the common cause of death amongst them.[2]

[1] The name in full is Abulcasem Khalaf Ebn-Abbas Al-Zaharavi; so that Albucasis and Alzaharavius are one and the same person: a fact known to Schenck, who, in the Elenchus Auctorum at the beginning of his *Observationes Medicæ*, says "Alzaharavius, qui est Albucasis." In more modern times this was rediscovered by Freind (*History of Physick*, London, 4th edition, 1750, Part II. p. 126).

[2] I am obliged to quote from a barbarous Latin translation published at Augsburg in 1519: its title is *Liber Theoricæ necnon Practicæ Alsaharavii*; the passage occurs in Tractatus xxxi, Sectio ii, Capitulum xv, Folio cxlv.

"De Passione fluxus sanguinis a quocumque locorum.

"Vidi in quibusdam regionibus casale quoddam dictum alkiria viros qui narraverunt mihi quoniam cum accidit in in corporibus ipsorum aliquod vulnus magnum indesinenter sanguis fluit ex vulnere quousque moritur: et recitaverunt

CHAP. II.

It has been a good deal doubted if this be a description of hæmophilia; but I think the probabilities are in its favour. The tendency to traumatic hæmorrhages, one of the most distinguishing notes of hæmophilia, is well marked: the tendency to hæmorrhage also exists in childhood and adult age; and it seems likely that it was hereditary, since it occurs amongst many inhabitants of a small village. No other disease but hæmophilia corresponds to these characters.

Passing by the very uncertain case of Alexander Benedictus,[1] published in 1539, we are indebted for

mihi super hoc quod quibusdam ex pueris suis cum fricaret manu gingivas cepit sanguis fluere ex illis donec mortuus est, Alius vero flebotomatus a minutore sanguinis non cessavit ex eo emanare, donec periit, Et universaliter eorum mors ut in pluribus contigit in hunc modum, Hæc est res quam nunquam et nusquam vidi nisi in casali prædicto, nec reperii hoc accidens ab aliquo antiquorum memorantium, nec scio ejus causam, et quod mihi videtur de curatione ejus est quod ille cui hoc accidit celeriter cauterizet locum, donec sanguis restringatur, et ego minime probavi hoc, et est apud me monstrum."

Alkiria is an Arabic word having precisely the same meaning as *casale*, a small village or homestead, from the Low Latin *casa*. (See Ducange's *Glossarium*).

This translation of Albucasis is by Sigismund Grimm: Haller calls it "versio pessima" in which severe condemnation every reader of the extract given above will agree. There is an Arabic MS. of the *Al-Tasrif* in the Bodleian at Oxford, but I regret that I have been unable to obtain a translation of this passage from the Arabic, for much light would have been thereby thrown upon the question whether Albucasis really refers to hæmophilia.

[1] Alexander Benedictus, *Omnium a vertice ad calcem morborum signa, causæ, indicationes, etc.*, Basileæ, 1539, Lib. iiii. Cap. iiii. p. 203.

"De sanguinis profluvio e naribus.

our knowledge of the next notice of hæmophilia to the learning of Professor Virchow,[1] who first drew attention to a passage in the writings of Philip Höchstetter,[2] a physician practising at Augsburg in the beginning of the seventeenth century. In this he speaks of a boy who shortly after his birth suffered a considerable hæmorrhage from the navel; later on in life he had repeated epistaxis, once at least bloody stools, and spontaneous ecchymoses. This is the best described of the older cases; few will be disposed to doubt its connexion with hæmophilia.

"........... Venetiis tonsor quidem cum in naribus pilos incommodos forcipe concideret, venulam incaute secuit, tantoque impetu sanguis erupit, ut sistendi modum medici plurimi non adinvenirent, et ille misere vitam finivit."

[1] Virchow, *Archiv f. path. Anat.* Bd. xxviii. p. 426.

[2] Philippi Hœchstetteri, Augustani, Physici Patriæ, *Rararum Observationum Medicinalium Decades Sex*, Francofurti et Lipsiæ, 1674, Tom. I. Decas ii. Casus Nonus, p. 170.

"Nati modo sanguinem fundens largius umbilicus et adulti ad hæmorrhagiam pronæ nares cum suggillatione.

"Puer quidam sanguinem ob non rite ligatum umbilicum recens natus copiosum fudit: mater remotis fasciis infantem commaculatum videns, perterrita in febrem et phrenesin incidens vitam morti cessit; puer non deterius habens; hæmorrhagiæ narium dum adolescit maxime fit obnoxius; ætatis nono copiosa fuit, ut adstantibus terrori esset. Ideoque adhibitis refrigerantibus et sanguinem sistentibus medicinis, narium stilla desiit, at feces cum sanguine fluenti et concreto prodiere, mixta, suggillataque, seu maculæ sanguineæ rubræ, post cæruleæ per cutim passim effloruere, in facie, pectore, dorso, artubus, quæ tandem flavæ factæ disparuere. Sequentibus annis, cum similis hæmorrhagia ac suggillatio adesssent, sequebatur scabies; quæ dum curatur mundantibus sanguinem et purgantibus corpus, promovetur hæmorrhagia. Quare undecimo anno ætatis venam adperui commode, teneram haud metuens ætatem."

CHAP. II.

There is another case belonging to the seventeenth century, which has been frequently quoted, but which has never before been traced to its original source. It is the case which is called by the Germans Lowthorp's, or Coxe's. It belongs, however, neither to the one nor to the other, but it is taken from the earlier volumes of the *Philosophical Transactions*. In a letter from a clergyman in Shropshire the illness and death of a little girl aged about 3 months is described. She was taken with a bleeding at the nose, and ears, and hinder part of the head, for three days. On the third day, the blood came more violently from the head: she bled also on the shoulders, waist, toes, bend of the arms, at the joints of the fingers and the fingers' ends. She died on the sixth day after the bleeding began. After the child was dead, there appeared in the places, where the blood issued, small holes like the pricks of a needle.[1]

This case was copied into Lowthorp's *Abridgement of the Philosophical Transactions*. Coxe, the Editor of the *Philadelphia Medical Museum*, commenting upon Smith's case, shortly to be referred to, quotes this case, with

[1] *Philosophical Transactions*, vol. ix, 1674, No. 109, p. 193. Dec. 14.

"Relation sent November 16. 1674. From a very credible and ingenious Person, Mr. Samuel du Gard, Rector of Forton in Shropshire to Dr. Ra. Bathurst Vice-Chancellor of the University of Oxford, and by him communicated to a Friend of his in London." The child died at Lilleshal in Shropshire about Candlemas, 1674: du Gard does not seem to have seen the child either alive or dead, and he says "this Accompt I had from the Mother of the Child, who is a very sober Woman; and she told it me with tears." He, however, saw some of the clothing stained with blood.

others, from Lowthorp's *Abridgement*. It does not seem to be one of hæmophilia; and the other two cases, quoted by Coxe, of Clopton Havers,[1] and Ash,[2] certainly are not.

There are two other cases in the same publication which have not yet, so far as I know, been referred to with respect to hæmophilia; they are deserving of some attention. One is a case[3] recorded by Dr. William Musgrave, F.R.S.; a Mr. H., formerly a servant to the Queen Dowager, had from his infancy to the 24th year of his age, a periodical hæmorrhage in one of his thumbs. The time of the eruption was about the full of the moon; the orifice was on the right side of the nail of the left thumb. At the age of 24 he seared this part with a hot iron: it stopped the bleeding for twenty years; but within a quarter of a year after it he fell into a spitting of blood, bringing up from his lungs vast quantities thereof. Thereafter he fell into a violent cholic, and with this he was ever after often troubled, as also with a spitting of blood.

The case, though curious, hardly belongs to hæmo-

[1] *Phil. Trans.* vol. xviii, 169¾, No. 208, p. 51.

In a letter to Clopton Havers, the case of a woman is described who about 3 months before her death began to bleed at the glandula lacrymalis: she bled till she died.

[2] *Phil. Trans.* vol. xv, 1685, No. 171, p. 989.

History of a man who began to bleed when 43 years old from the end of his fore finger; this bleeding returned about every three weeks.

[3] Musgrave, *Phil. Trans.* vol. xxii, 1701, No. 272, p. 864.

The case is quoted by Lefebvre with reference to the phænomena of Stigmatisation (*Louise Lateau de Bois d'Haine*, Louvain, 1870, p. 116).

CHAP. II. philia. There would be no doubt as to the case which follows, did there exist any account of hæmorrhages before the 24th year of the patient's life: but unfortunately there is no mention of the state of the man's health before this time. As the earlier volumes of the *Philosophical Transactions* are somewhat difficult of access, I give the whole of the description, thinking that it may interest some.

"In the Month of *January* 1729. *Daniel Goddard*, a Gardener, about the Age of Twenty-four Years, at *Wisbech* in the Isle of *Ely*, *Cambridgeshire*, happened of a slight Puncture from a rusty Nail in the Sole of his Right Foot. And, notwithstanding there was not wounded any Tendon, or Blood-Vessel, larger than small Branches of Veins, the whole Foot was immediately swelled to a very unusual Degree, without any Fever, or other apparent Cause for it. It was also attended with great Pain, and an extraordinary Pulsation upon the Part, as in the Wounds of Arteries; and so distended as if the Blood would burst out of its Vessels.

"Accordingly, after Two Days, upon opening a superficial Sinus, to inlarge the Wound, there rushed out immediately such an obstinate Flux of Blood, as would not yield to any styptic Means, longer than the Bandage was holden on by some strong Hand. And, although, by this Incision, no Vessels were wounded, but Capillary Veins; yet this *Hæmorrhage* continued to shew itself as violent as at first, for Six Days successively, whenever the necessary Means were relaxed. Upon which, for the sake of *Revulsion*, the Patient had a Vein opened on the Arm of the opposite Side; and it had such a sudden and surprizing Effect, that

the Flux of Blood in the Foot instantly ceased, and the Wound healed very soon without any further Trouble; but the Flux of Blood, consequent upon Venesection, became equally as difficult to restrain, as that in the Foot, for the Space of Four Days; all which time it would have continued to flow most violently without the strictest Bandage, as the same Care of the Hand, as before. Perhaps the Period of this *Hæmorrhage* might have been much longer, if I had not suffered the Ligature on the Arm to be loosened now-and-then, as I judged the Redundancy of Blood required, for the sake of some Evacuation, at each time. After the Bleeding, he soon recovered his Strength so as to do his Business in the Gardens; and continued very well till the Month of *March* 1730. About the middle of this month, he complained of Sleepiness, and a particular Heaviness all over his Body; which was followed, in Three Days time, by a violent *Hæmorrhage* from the *Nose*. This Flux, in spite of all Means being tried, except Venesection, continued Seven Days, and could never be totally stopped, all this time, for one Hour together. He recovered again in a very short time, and was able to work in the Summer-season, without any Complaints, till *October* following. Then the *Hæmorrhage* returned again at the *Nose*, as before, with all the same Circumstances, and in Defiance of all Endeavours, continued the Period of Seven Days. Thus it returned in like manner of Bleeding, by *Stools*, in the Middle of *March* 1731, and continued to discharge this Way great Quantities of Blood, in one Motion, and sometimes two Motions every Day for Seven Days together, in Opposition to the most efficacious Restringents. Also it made its

CHAP. II. regular Return by vast Profusions of Blood from the *Intestines*, in the Beginning of *October* following, to the End of the first Period of Seven Days, without Gripings, or any such uneasy Sensations. Thus, again, it kept as orderly Returns about the Vernal and Autumnal Equinoxes of the Years 1732, 1733, with vast Profusion of Blood by Stool, for the usual Term of Seven Days, agreeing in all Circumstances with the preceding Years. Likewise at, or very near these two grand Seasons, in the years 1734, 1735, this habitual *Hæmorrhage* broke away by the *Kidneys and urinary Passage;* and still constantly, for these Two Years, kept its old stated time of Seven Days, without any other Variation.

"This young Man was seized in *Dec.* 1735, with the *Small-pox*, of the Distinct Kind, which produced such a Change in his Constitution, that he escaped those periodical *Hæmorrhages*, or any other spontaneous Evacuations equivalent thereto, for the Two Seasons of the Year 1736; and remained in very good Health till *Christmas* following, being above Thirteen Months free from any Symptoms of his old Eruption. But, upon *December* the 27th, without any previous Notice of Heaviness and Sleepiness, the *Hæmorrhage* returned by the *urinary Passages;* but much more favourably, and continued only Three Days. Again, on *May* the 13th following, 1737, he then felt the previous Warnings, and bled again by Urine to the 20th of the same Month; with this Difference, that for Three Days the Urine was only Coffee-coloured, but afterwards, for Four Days longer, every Discharge resembled an Effusion of Blood from a Vein just opened.

He presently recovered his Strength, even although the Air was exceeding warm at this Time; and I saw him Five Months after, very robust and healthy, and, as he told me himself, was free from all kinds of Tendency towards his old Complaint. But he had always the Appearance of too much Fulness, though I am of opinion, that his Constitution did not suffer so much as might reasonably be imagined, from such prodigious *Hæmorrhages*. Of my own Knowledge, he had no Return of his Bleeding, or any thing like it, the ensuing Autumn; but remained perfectly well all the following Winter Season. Afterwards I had no Opportunity of making further personal Inquiries, but was informed by an intelligent Man, that in *March* 1738, this unfortunate Person got a slight Wound again, somewhere upon one of his Legs, which proved equally as difficult, with respect to the Flux of Blood, as the first Puncture in his Foot. And, whether from a too strict a Restraint of the *Hæmorrhage*, or for want of Venesection, he fell into very violent Convulsions for Four or Five Days, and died in a manner like Suffocation, from too much Redundancy of Blood.

"As this *Hæmorrhage* never once depended upon any other Distemper, or observed any regular Concurrence with the Revolutions of the Moon, it appears to be a very extraordinary simple *Plethora*. During the Four Years that this Flux of Blood came from the Nose and Intestines, the Urine was never of a higher Colour than Amber; nor was there any Symptom of a Fever by the Pulse, or otherways, for the whole Term of the Disorder."[1]

[1] Banyer, *Phil. Trans.* vol. xlii., 1743, No. 471, p. 268.

CHAP. II. There is also a possible case of hæmophilia recorded by Macquart, of a young soldier, who had been subject to repeated epistaxis from his earliest infancy, and who, during convalescence from pneumonia, suffered a severe attack of hæmaturia.[1]

The next notice of the disease is by Sir W. Fordyce, who describes a family in Northamptonshire, the father, a daughter, and sons who suffered from repeated hæmorrhages: it is thought doubtful by some if the case of the drummer boy also described in the same place belong to hæmophilia.[2] Ten years after Fordyce's publication there appeared in Germany two notices of the disease neither of which I have been able to see. One is by a writer in the *Medicinische Ephemeriden*, p. 267, published at Chemnitz in 1793; the other is by Rave,[3] published in 1798. This latter is considered by Grandidier, from whom I borrow the reference, to be a disease intermediate between hæmophilia and scurvy.

Next follow a series of observations at the beginning of the present century by the North American physicians. Otto, in 1803, described a family in New England in which hæmophilia had existed for 70 or 80 years:[4] and in 1813, a branch of the same family was described by Hay.[5] In 1805, there was published a

[1] Macquart, Richard de Hautesierck's *Recuïl d'observations de Médecine des Hôpitaux militaires*, Paris, 1772, t. ii. p. 293.

[2] Fordyce, *Fragmenta Chirurgica et Medica*, Lond. 1784, p. 41.

[3] Rave, *Beobachtungen und Schlüsse aus der praktischen Arzneiwissenschaft*, 2. Theil, 1798, p. 12.

[4] Otto, *Medical Repository*, New York, 1803, vol. vi. p. 1.

[5] Hay, *New England Journal of Medicine and Surgery*, Boston, 1813, vol. ii. p. 221.

letter by E. H. Smith, written at New York, April 9th, 1794: in this there is described the case of a little boy who used to bleed considerably a few days before his birthday; and which bleeding always stopped upon his birthday. He died of hæmorrhage 5 days before he was four years old.[1]

Unless a case described in the *Esprit des Journaux* for January, 1805,[2] be one of hæmophilia, the next European notices of the disease are by the Editor of *Sammlung auserlesener Abhandlungen*[3] in 1805, and by Consbruch[4] in 1810, followed by careful clinical and *post-mortem* observations by Blagden[5] in 1817 and James Wilson[6] in 1819.

The next publication marks the transition from the records of isolated cases to an attempt at the scientific description of the disease. In 1820, Nasse published his paper *Von einer erblichen Neigung zu tödtlichen Blutungen*,[7] in which most of the published cases are collected, and a general view is given of the disease. Schönlein's influence at this time began to be felt. He proposed a name for the disease and introduced it into systematic Pathology. Under his teaching, many inaugural dissertations on hæmophilia were published at

[1] E. H. Smith, *Philadelphia Medical Museum*, vol. i. p. 284.

[2] This publication, I regret, I have been unable to see.

[3] *Sammlung auserlesener Abhandlungen*, 1805, Leipzig, Bd. xxii. Stück ii. p. 275.

[4] Consbruch, Hufeland's *Journal*, Bd. xxx. Stück v. p. 116.

[5] Blagden, *Med.-Chir. Trans*, Vol. viii. p. 224.

[6] James Wilson, *Lectures on the Blood*, &c. Lond. 1819, p. 410.

[7] Nasse, Horn's *Archiv*, 1820, Mai-Juni, p. 385.

CHAP. II. Würzburg and Berlin. In 1829, Rieken[1] published his monograph which added greatly to the general knowledge of the disease, although it contains some opinions which cannot now-a-days be endorsed.

After 1820, the history of hæmophilia becomes almost entirely German. The United States, after affording one or two more examples of the disease,[2] disappear almost completely from the literature. England, indeed, collects a great mass of material of single cases, which no one, however, takes the pains to arrange or digest. In France, the disease attracts but a fitful attention; and in the rest of Europe it seems to be unknown or disregarded.

But in Germany from 1830 to 1850, not only are a great number of cases collected, but tolerably complete descriptions are met with in the text books of Schönlein, Canstatt, Neumann, Fuchs, &c. Two theories as to the pathology of hæmophilia prevailed: one, the favourite doctrine of Schönlein, that the disease was related to cyanosis and malformation of the heart: the other, that it was a form of anomalous gout or 'scrofula.'

In 1849, Wachsmuth[3] published a very good monograph on hæmophilia, containing many new observations and thoughts: and a year after, Lange's posthumous statistical researches were published in Oppenheim's *Zeitschrift*; and, so far as I am able to judge, this work was done with much care and discretion. In 1854,

[1] Rieken, *Neue Untersuchungen in Betreff der erblichen Neigung zu tödtlichen Blutungen*, Frankfurt a.M. 1829.

[2] The brothers Buel, Coates, and Hughes.

[3] Wachsmuth, *Die Bluterkrankheit*, Magdeburg, 1849.

Virchow gave a good account of the disease in his *Handbuch der speciellen Pathologie und Therapie*: and in the following year Grandidier published his treatise, *Die Hämophilie*, supplemented by a report in Schmidt's *Jahrbücher* for 1863. Of late some important cases have been published: by Lemp[1] in 1857, containing the account of a *post-mortem* examination made by Professor Virchow; by Gavoy,[2] in 1861, containing an account of the microscopical examination of the blood vessels and an analysis of the blood; and lastly by Otte[3] in 1865, containing observations upon the influence of the weather on the occurrence of the bleedings, and a further analysis of the blood. CHAP. II.

1 Lemp, *De Haemophilia nonnulla*, Diss. Inaug. Berol., 1857.

2 Gavoy, *L'hémophilie, ou diathèse hémorrhagique*, Thèse de Strasbourg, 1861.

3 Otte, *Ueber die Bluterkrankheit*, Leipzig, 1865.

CHAPTER III.

ÆTIOLOGY OF HÆMOPHILIA.

When the first descriptions of this disease were published, it was thought that hæmophilia occurred amongst the boys only of a family, and that the girls were exempt.[1] By the gradual collection of cases, however, this assumption has not been maintained; although women are far less disposed to the disease than men. Lange,[2] for instance, collected in 1849 all the published cases, and he found that the numbers were 227 or 229 boys to 31 girls, a proportion of 7 : 1. But in 1855, Grandidier[3] found that the numbers had risen to 452 boys and 32 girls, an increase of one case only amongst women: this is a proportion of 14 : 1. But in 1863, the same writer[4] found that the ratio had fallen, and was as 11 : 1. I believe that this lowering of the proportion is caused by the admission of cases that have small claims to be considered hæmophilia: indeed in Grandidier's first list there are several cases that must be looked upon with great suspicion, such as instances of umbilical hæmorrhage in the new born, or uncomplicated menorrhagia in adults.

[1] Otto, *Medical Repository*, New York, 1803, vol. vi. p. 3.
Nasse, Horn's *Archiv*, 1820, Mai-Juni, p. 390.

[2] Lange, Oppenheim's *Zeitschrift*, 1851, Bd. xlv, Statistische Untersuchungen über die Bluterkrankheit, p. 157.

[3] Grandidier, *Die Hämophilie*, 1855, Leipzig, p. 87.

[4] Grandidier, Schmidt's *Jahrbücher*, 1863, Bd. cxvii, p 335.

The women also who are the subjects of hæmophilia rarely present typical instances of the disease. The danger to life is infinitely less than in the opposite sex. Grandidier, indeed, says that 16 out of the recorded cases have fallen victims to hæmorrhage;[1] but from the circumstances mentioned above, these figures must not be received with too implicit a faith. Most of them have died from bleedings from the genital organs, and Wachsmuth has recorded a case, where the rupture of the hymen on the marriage night caused the death of the bride from hæmorrhage.[2]

The disease, also, affects women with a lower degree of intensity than men: they do not bleed more than is usual when wounded, and the disposition may limit itself to the occurrence of spontaneous hæmorrhages, or to early, abundant, and prolonged menstruation. Floodings are common both after delivery, and at the time of the cessation of the catamenia. The mother and daughter, mentioned by Nasse,[3] belonging to a bleeder family, died of profuse floodings about the climacteric.

Hereditary disposition is the best ascertained cause of hæmophilia. Out of 98 families, there was a disposition to hæmorrhage in the parents, grandparents, or cousins, in 52.[4] Of the remaining 46 families, the parents enjoyed good health in 20, but in 26, they suffered from gout, scrofula, whatever the exact meaning of that term may be, syphilis, lung and heart disease.

[1] Grandidier, *loc. cit.*

[2] Wachsmuth, *Die Bluterkrankheit*, Magdeburg, 1849, p. 9.

[3] Nasse, *op. cit.*, p. 426.

[4] Grandidier, Schmidt's *Jahrbücher*, Bd. cxvii, p. 336.

CHAP. III. Grandidier is inclined to think that the mothers are more often in bad health than the fathers.[1]

I think that the disease may be traced to hereditary transmission oftener than is allowed. When, for example, all the boys, or nearly all the boys of a family are bleeders, it would seem more likely that there is an hereditary taint rather than a generation *de novo* of the disease. This, of course, may be rebutted when there exist records of the family for many generations past; but among the poor, nothing is usually known before the time of the grandparents, and often not so far back as that. It will be seen that the disease may make its appearance at long intervals, remaining latent, if I may use the expression, in the women of the family for two or more generations. When the disease cannot be traced to transmission, but little is known with certainty as to other causes. Some have carried the idea of hereditary disposition to an extreme, and asserted that all bleeders have a common ancestry. But this is plainly impossible.[2] Others have thought that the disease arises when intermarriage of near relations is allowed;[3] and support seems to be given to this view from the apparent greater prevalence of the disease in Germany where the marriage of cousins is so little

[1] Grandidier, *loc. cit.*

[2] The case of Heymann's (*Arch. f. path. Anat.* Bd. xvi, p. 182) of a Mussulman family in Sumatra would have proved this point conclusively, had the writer stated that there had been no infusion of European blood; for the Dutch had once a factory in the island.

[3] Rieken, *Neue Untersuchungen in Betreff der erblichen Neigung zu tödtlichen Blutungen,* Frankfurt a.M. 1829, p. 102.

Heyfelder, *Medizin. Zeitung (Verein's),* 1833, p. 216.

discouraged: it is also more common among the Jews, who are obliged to intermarry. Rieken[1] has tried to prove some relationship in hæmophilia to gout. But, in truth, nothing is known of the circumstances which commonly surround the production, *de novo*, of this disease. That the disease can be produced in a healthy child by food or external agencies is extremely unlikely. Yet such a case has been brought forward by Guépratte:[2] a healthy boy in the island of Guadaloupe was suckled by a black woman, already exhausted by three wet-nursings following close on each other; she also fed the child badly with much fruit, and lived in a damp low hut. The boy acquired all the appearances of hæmophilia, including a swelling of the ankle; but recovered after a long dietetic treatment. The description of the case to which I have had access, leaves upon the mind the impression of purpura or some allied disorder, and not of hæmophilia. Such a rapid recovery has never yet been seen in this latter disease.

A case has been recorded by Mutzenbecher, in which it is supposed that the disease was generated *de novo*.[3] A strong and healthy boy was born of healthy parents, who were quite ignorant of any disposition to excessive bleedings in any of their relations. When the child was 9 months old, and still being suckled, the mother barely escaped being outraged by some French soldiers in a wood near to her home. Greatly frightened, the woman fainted on reaching her house; and when she had scarcely recovered her senses, she gave her child

[1] Rieken, *op. cit.* p. 87.

[2] Guépratte, Canstatt's *Jahresbericht fuer* 1844, Bd. iii. p. 291.

[3] Mutzenbecher, quoted by Grandidier, *op. cit.* p. 100.

CHAP. III. the breast. From that moment the child lost its healthy look, and shortly after showed symptoms of hæmophilia, ecchymoses and bleedings, traumatic and spontaneous. Two other boys, also bleeders, were also born of this woman.

Even if this be a case of the generation of hæmophilia *de novo*, there is little evidence to show that the mental emotion suffered by the mother was the commencement of the disease. Hæmophilia seldom shows itself before the end of the first year; and it may probably have been incubating in this child, until some exciting cause brought out symptoms. Again, the woman bore two other children, bleeders: a fact which makes a hereditary transmission probable; and wherefore, then, seek for a cause of hæmophilia in the ingestion of a small quantity of milk, secreted while the nurse was under the influence of depressing emotion? a cause which seems quite unequal to the production of so great a result, nothing less than a complete revolution in the constitution of the infant.

There is also a case recorded by André, of a woman who during her third pregnancy saw one of her maids bleeding from a wound on the head. She was delivered of a daughter who died, when 10 weeks old, of a bleeding from the scalp and ends of the fingers. Two boys were afterwards begotten, who both died, when 10 weeks old, of hæmorrhage. Here again, children with a disposition to bleed were begotten long after the first mental disturbance; and further, the children did not live long enough to make the diagnosis of hæmophilia unquestionable.[1]

[1] André, Schmidt's *Jahrbücher*, Bd. lxxii. p. 142.

It is well, nevertheless, not to lose sight altogether of the influence of the emotions, specially of the depressing emotions, in the production of hæmorrhage. A sudden great fear is not uncommonly the starting point of a hæmorrhagic disposition in women: and the emotions of grief and anger may be followed by hæmorrhages.[1] I believe that the emotions have a far greater influence upon the tissues than is generally thought. CHAP. III.

The daughters of a bleeder family are to a great extent protected against hæmophilia. But though they are themselves so slightly liable to the disease, yet they possess in a very high degree the faculty of transmitting hæmophilia to their sons. The women may appear perfectly healthy: they may marry perfectly healthy husbands; and yet bear a family all the boys of which shall be bleeders. Something like this is not very unfrequently seen in gout, a disease which rarely attacks women. The father and brothers may be gouty: and a daughter, remaining herself free from the disease, may bear a son who shall have well-marked gouty paroxysms, no other hereditary taint, and no exciting cause, being apparent.

When women, who are themselves the subjects of hæmophilia, bear children, their sons appear to be neither more nor less liable to the disease than if their mothers had sprung of a bleeder family, but had been them-

[1] Joseph Frank, *Praxeos Medicae Universae Praecepta*, pars ii. vol. ii. sect. ii. De Amore effraeno, Edit. Sec. Taurin. 1821, p. 255. See also Haller, *Elem. Phys.* lib. xvii. sect. ii. § 6. *et seq.;* Gendrin, *Traité philosophique de Médecine pratique*, Paris, 1838, t. i. p. 57; and Lordat, *Traité des Hémorragies*, Paris, 1808, p. 84. The influence of the soul formed an important part of Stahl's theory of hæmorrhages.

CHAP. III. selves free from the disease. Reinert records two cases of this kind, which are, indeed, rare; in one, the woman bore 6 sons and 2 daughters, of whom only 3 sons were bleeders; in the other, the woman bore 4 sons and 2 daughters, and only one son was a bleeder.[1]

When the men of a bleeder family, themselves the subjects of hæmophilia, beget children, it is not often that they transmit the disease directly to their children. There are several cases on record where the disease has passed from father to son;[2] but it is not the rule, and in some of these cases, the father was not sprung of a bleeder family and the account given of him scarcely warrants the assumption that he was the subject of hæmophilia. Transmission through the father directly to the son is not uncommonly seen when the father's brothers are bleeders, but he himself has escaped.

But although the children of a man, subject to hæmophilia, do not themselves suffer, yet some of the grandsons, the daughter's sons, are almost sure to be affected; the sons' sons escape, but the disease reappears in the grandsons by the daughters, their sisters again transmitting the disease to their sons. Do the grand-daughters by the sons pass the disease on to their offspring? and do the brothers of bleeders, themselves free from hæmophilia, transmit the disease by their daughters? There are, unfortunately, no very clear observations on these points. Most of the histo-

[1] Reinert, *Ueber Hämophilie*, Diss. Inaug. Göttingen, 1869, pp. 4—6.

[2] Notably the case described by Steinmetz (Rust's *Magazin*, Bd. xxvii. Heft. ii. p. 378), where the disease descended in a Jew family from the father to his son, and thence to the grandson.

ries are taken from the families of the artizan class, and these, as already remarked, are unsuited for any observations as to descent.

Through how many generations hæmophilia may be transmitted is unknown; and until the disease have been under continuous observation for a longer time, no sufficient data can be obtained. In the village of Tenna in the Swiss canton of Graubünden, there are two families of bleeders which have certainly existed since 1770, and probably for some time before this date. The tradition in the village is that a young man was condemned to death for a petty theft by a judge who was his godfather; and that at the supreme moment the thief called down a curse upon the judge, and upon his children after him. Be the value of this tradition what it may, it points to a time when the two families were closely allied: and in 1770 they were not related to each other.[1] It thus seems probable that the disease has lasted for many years before the first written records. Of two of the American families there are accounts which extend through 4 or 5 generations[2] and Kuester says that the sons in the family of his patient had been bleeders as far back as they could remember.[3]

It seems improbable that the disease, once established in a family, should ever die out; but there is one in-

[1] Grandidier, *op. cit.* p. 21.

[2] Hay. *New England Journal of Medicine and Surgery*, Boston, 1813, vol. ii. p. 221. From 1715 to 1810.

Hughes, *American Journal of Medical Science*, 1833. vol. xi. p. 542.

[3] "Ein Curgast, 28-30 Jahre alt, ... erwiederte wie alle männlichen Glieder seiner Familie seit undenklichen Zeiten Bluter wären" (Küster, Caspar's *Wochenschrift*, 1847, p. 282.)

CHAP. III. stance recorded in which the disease has been reported to be insensibly disappearing.[1]

From a table of 52 families given by Grandidier in which the number of children is stated, it appears that all the sons were bleeders in 24, that is, in nearly half the families.[2] In 3, all the children, sons and daughters, were bleeders; but in these 3 families there was only one daughter. In 13 out of 54 families, one or more of the daughters, usually, however, only one out of several, were the subjects of hæmophilia. As a rule, those members of the family, whether men or women, who are not themselves subject to bleedings, enjoy good health.

Wachsmuth[3] was the first to notice the uncommon fertility of the women belonging to bleeding families. In 12 families there were no less than 112 children, giving an average of nearly 10 children for each family, a number far above the usual proportion. The mortality amongst the children is very great, and it is perhaps to compensate for this that so many are born. Those in the family who are not the subjects of hæmophilia do not seem to be more liable than other children to death at an early age. Lange[4] found that of 64 such children, 13 were dead at the end of the first year, and 14 at the end of the fifth, a mortality by no means high.

It has appeared to me, in looking over the recorded cases of hæmophilia, that, where all the boys are not

[1] *Journal des Progrès*, 1828, vol. xi. p. 244.

[2] Grandidier, *op. cit.* p. 97.

[3] Wachsmuth, *op. cit.* p. 35.

[4] Lange, *op. cit.* p. 165. It is not clear whether Lange meant that 14, or 27, out of the 64 were dead at the end of the 5th year.

the subjects of the disease, the first born are more exempt than the others. In the present state of matters, there are too few cases given in sufficient detail to be capable of being used for statistical purposes: but I venture to draw the attention of observers to this point in order that it may be either disproved or confirmed.

It is a matter open to discussion whether hæmophilia be more frequent in one country than another. There can be no doubt, however, as to the country in which the largest number of cases has been described. Germany has recorded nearly 50 per cent. of the known cases; England, less than 20 per cent. including a few Scotch and Irish cases; France, the United States of North America, and Switzerland, about 10 per cent. each. A few cases have been described by German physicians in the German provinces of Russia. One or two cases have been reported from the Scandinavian kingdoms. But Spain has afforded no case since the days of Abulcasis.[1] In Italy, Turkey, and the rest of the civilized world, the disease seems to be unknown, or to be disregarded. A few years ago, the history of a bleeder family in Sumatra was published by a German physician:[2] but this is the only case from Asia that has ever been brought forward.

From the large proportion of cases which have been recorded by German, English, and American writers, it has been thought by some that hæmophilia is a special

1 This writer was born and died near Cordova, in Spain: it seems, therefore, more probable that his case was observed in that country, than, as so many authors assert, in Arabia.

2 Heymann, *Arch. f. path. Anat.* Bd. xvi. p. 182.

CHAP. III. inheritance of the Teutonic race. Some light may be thrown upon this hypothesis by a study of the history of the disease. Nasse first published his monograph on hæmophilia in Horn's *Archiv* for 1820: he was a professor in the University of Bonn, and the Bonn students were thus familiarised with the disease, and for several years after, more cases were published from the provinces watered by the Rhine and the Main, than from any other part of Germany: the Bonn students had become practitioners, and recorded their cases. The influence of Schönlein, also, at Würzburg helped in the same direction, as testify the numerous inaugural dissertations on hæmophilia published at Würzburg during the time that Schönlein held the chair of pathology in that University. The cases came from the Rhine and the Main so exclusively, that in 1847 it could be said that the home of hæmophilia was in the vineyards. But wait another ten or twenty years, and the disease is found to be spread almost equally over Germany. The reason of this is plain: the disease has become widely known; the monographs of Lange, Wachsmuth, and Grandidier, and the descriptions of the disease in the handbooks, especially in Virchow's great work, have awakened an interest in hæmophilia throughout Germany. Reports also come in from German physicians, living in Russia and the Indian Archipelago, countries thought to be free from the disease.

Again: My friend Mr. Swanzy informs me that hæmophilia is not an extreme rarity in the hospitals of Dublin; and yet there are only two Irish cases, so far as I know, on record. In like manner, Dr. Gross, speaking in 1845

of hæmophilia, could say that "almost every practitioner must have noticed cases of this description,"[1] and yet the United States, since the very beginning of this century, have afforded but one or two cases at the utmost. These facts make the probability great that the number of recorded cases depends not upon the frequency of hæmophilia in a given country, but upon the previous education of the medical men, and the interest which they take in the disease.

No conclusions either can be drawn from the absence of any description of hæmophilia in the books which treat of the climate and maladies of a country.[2] In the Indian Sanitary Reports it is very unlikely that any mention of the disease should occur; the statistics are arranged according to the Nosology recently published by the London College of Physicians; and this work does not admit hæmophilia into its lists of disease.

Another fact, opposed to the idea that hæmophilia is confined to the Indo-Germanic race, is its prevalence amongst the Jews, a certain percentage of the German cases having occurred in this Semitic nation. The notion that all bleeders are sprung of a common stock is plainly an impossibility, when the wide diffusion of the disease is considered.

[1] Gross, *Elements of Pathological Anatomy*, Philadelphia, 1845, Sec. Ed. p. 65.

[2] A crucial instance of this may here be noticed. Grandidier (*op. cit.* p. 46) quotes a work by Waitz, published at Amsterdam in 1843, upon the diseases of children in the Indian Archipelago to prove the absence of hæmophilia in that region. In 1859, Heymann (*Arch. f. path. Anat.* Bd. xvi. p. 182) published an account of a family of bleeders in Sumatra, in whom the disposition could be traced back for 3 generations.

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Hæmophilia does not seem to select any one class in social life more than another: it occurs in the families of the peer[1] and the pauper. Most of the recorded cases, as might be expected, come from the middle and lower classes.

The geographical distribution of hæmophilia has been already discussed: it appears in the low sandy plains of North Germany, and in the Swiss mountains, 5000 feet above the level of the sea, as well as in the valleys and watersheds of the Rhine and the Main. It does not seem to be influenced by food; since the inhabitants of Tenna, where hæmophilia might almost be called endemic, live chiefly upon meat and milk; nor are any hygienic conditions known to have any share in the generation *de novo* of the disease.

[1] I have heard of a case in the family of an English nobleman; and Charles IX. of France is thought by some to have been the subject of this disease.

CHAPTER IV.

SYMPTOMS OF HÆMOPHILIA.

The first signs of the presence of hæmophilia are, in nearly every case, given in the period of childhood, that is, from the time of birth to the commencement of the second dentition. Grandidier[1] found that out of 65 boys, positive signs of the disease had appeared in 62 before the end of the tenth year. Out of 70 cases, the disease first appeared in 48 towards the end of the first year, the beginning of the first dentition.[2] Hæmophilia may indeed show itself immediately after birth; as when a child, born of a bleeder stock, almost bleeds to death after ritual circumcision. Hæmorrhage on the falling off of the stump of the umbilical cord is not often seen in hæmophilia: out of 185 bleeder families, and 576 individual bleeders, it occurred in only 9 families, and 12 individuals.[3] Virchow does not give the authority upon which he states that bleedings may take place during the birth of the child:[4] and Nasse's remark, that the disease already exists in the fœtus,[5] although highly probable, cannot be proved. The disease is latent at the time of birth, but does not manifest itself until provoked by some injury; and it most usually

[1] Grandidier, *op. cit.* p. 91.

[2] Grandidier, Schmidt's *Jahrbücher*, Bd. cxvii. p. 335.

[3] Grandidier, *Die freiwilligen Nabelblutungen*, Cassel, 1871, p. 84.

[4] Virchow, *Handb. d. spec. Path. u. Ther.* Bd. i. p. 264.

[5] Nasse, quoted by Lange, *op. cit.* p. 186.

CHAP. IV. appears about the end of the first twelvemonth, because the infant then begins to be put upon its feet, and is allowed to crawl about, being thus exposed to injuries from which it was before protected when carried in the arms. It is not uncommon to find that no symptoms of hæmophilia have been noticed until a considerable injury draws attention to the great loss of blood. This is, of course, more common among the neglected children of the poor than in the families of their betters.

The latest age, at which it has been asserted that hæmophilia has first appeared, is between 21 and 22. Both father and son became subject to profuse bleedings first at this age, and both died of hæmorrhage.[1]

The joint affections, which are so prominent a feature in typical cases of hæmophilia first appear between the commencement and the completion of the second dentition, that is, between the 7th and 8th years of life, and the 13th or 14th. Very rarely is the first appearance delayed till after puberty.

Persons who are the subjects of hæmophilia have often light hair and eyes. Sometimes, however, the hair and eyes are black or dark brown. Their skin is thin and transparent, and the veins are plainly seen. There is nothing constant as regards their stature or muscular strength. When they are not suffering from the effects of hæmorrhage or joint disease, they look well and healthy; and there is then

[1] Steiner, quoted by Grandidier, *op. cit.* p. 91. From Grandidier's account, neither case seems to be one, about the diagnosis of which there could be no doubt; but the author has chosen to hide his light under the bushel of an inaugural dissertation, and I have therefore been unable to procure or see the original.

nothing by which they may be distinguished from other healthy persons.[1] Physical examination detects nothing unnatural in the chest or belly: in one or two cases the spleen or liver has been thought to be enlarged,[2] but this is quite the exception. Grandidier is of opinion that a stronger and more diffused impulse of the heart is common.[3]

Many observers agree in one point which is, perhaps, the most singular feature of this very interesting disease: these patients are often of considerable intellectual capacity; and it is stated that, as children, they distinguish themselves at school.[4]

[1] Otto (*Medical Repository*, New York, 1803, vol. vi. p. 3.) says that "some persons, who are curious, suppose they can distinguish the bleeders (for this is the name given to them) even in infancy; but as yet the characteristic marks are not ascertained sufficiently definite." And Hay: (*New England Journal of Medicine and Surgery*, Boston, 1813, vol. ii. p. 225) "The great grandmother of Mr. Hartshorne's children, pronounced them bleeders in their infancy; her predictions, with regard to her bleeding descendants, have always been verified." Dequevauviller (*De la disposition aux hémorrhagies, etc.* Thèse de Paris, 1844, No. 87, *passim*) seems to think that a stature of some height, a fine skin, small muscular development, absence of fat, scanty hair, and a transparent sclerotic are always to be found when any disposition to capillary hæmorrhage exists. As a rule, the statement in the text holds good.

[2] Beier, *De Hæmophilia*, Diss. Inaug. Berol. 1864. p. 28. "Hepatis lienisque volumen auctum."

Waterhouse, *British Medical Journal*, 1870, vol. ii. p. 680. The spleen enlarged, liver diminished in size.

Schünemann, *Arch. f. path. Anat.* Bd. xli. p. 289. Liver and spleen enlarged, *post mortem*.

[3] Grandidier, *op. cit.* p. 82.

[4] Lange, *op. cit.* p. 202. I feel much inclined to regard this belief as a myth: it was first introduced by Krimer, who noticed in his patients a great talent for mechanics and music; the observation has been imitated by his successors.

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Wachsmuth has pointed out two forms of hæmophilia, an erethetic and an atonic form.[1] In the erethetic form, the patients have mostly dark hair, sometimes, however, light; blue or dark eyes; delicate white skin through which the veins are clearly seen; but sometimes there is an increase of pigment in the skin. The figure is often slender, but the muscles powerful; temperament sanguine; as a rule cheerful and good-tempered, they are liable to outbreaks of violent passion. Their intelligence and memory are good, and they are fond of music, drawing, and mechanics. In the atonic form, the patients have light hair and eyes; there is little disposition to the formation of pigment; the constitution resembles that in 'scrofula'; temperament phlegmatic; they are indolent and listless, while their mental faculties are usually below par.

The disposition which some authors[2] have remarked in these patients to occupy themselves with womanish pursuits, arises clearly not from the hæmophilia but from the care that their friends take to ward off all injuries: hence the boys are not allowed to join in the ordinary sports of their age, and this, doubtless, impresses a somewhat feminine character upon them. When they attain puberty, there is often little or no beard, and only a few short hairs on the upper lip; about the pubes, the hair is as abundant as usual.

The functions of animal life are, as a rule, well performed. Digestion and assimilation seem to be

[1] Wachsmuth, *op. cit.* p. 33.

[2] Especially Krimer, Horn's *Archiv*, 1820, Mai-Juni, p. 409.

quite natural. Two analyses of the urine have shown a diminution of the urea and uric acid:[1] but these were both made by the old method of estimating the percentage of urea &c. in a given specimen; and they do not appear to have been repeated. Finger found no diminution of the urea in one of his cases.[2]

There are three well-marked degrees of hæmophilia. The first presents the most typical and characteristic form: in it there is a tendency to every kind of hæmorrhage, traumatic or spontaneous, interstitial or superficial. The tendency to the swelling of the joints is also well marked. This form is scarcely ever seen in women, but it is by far the most common among men. The second degree of the disease is infinitely less intense; spontaneous hæmorrhages from the mucous membranes only are present; neither traumatic hæmor-

[1] In Grandidier's case (*op. cit.* p. 35) of a Jew bleeder, aged 14, the analysis was made by Wild: there was no albumen, sugar, or hæmatin present. 1000 parts contained:

Water	968·792
Urea	18·75
Potash Sulphate	2·141
Soda Sulphate	2·083
Soda Phosphate	1·462
Lime & Magnesia Phosphate	·674
Sodium Chloride	2·96
Ammonia Phosphate & Chloride	1·92
Extractives	·815
Uric Acid	·403

In Schliemann's case (quoted by Grandidier, *op. cit.* p. 36) of a bleeder, aged 13, the analysis of the urine by Raub in Würzburg gave the following results: 1000 parts contained:

Water	973·8813
Urea	5·215
Potash Sulphate	2·634
Lime Sulphate	·0065
Soda Phosphate	·274
Lime Phosphate	·108
Magnesia Phosphate	1·071
Sodium Chloride	5·498
Ammonium Chloride	1·577
Extractives	7·929
Mucus	·677
Albumen	·0007
Uric Acid	·0065

[2] Finger, Schmidt's *Jahrbücher*, Bd. cxvii. p. 330.

CHAP. IV. rhages, nor ecchymoses are met with; and the joint affection is absent, or represented only by rheumatic pains. When hæmophilia occurs in women, it usually assumes this form; and it may sometimes also be seen in boys and men. The third is the lowest degree of the disease, the liability to spontaneous ecchymoses being the only sign of its presence: it takes this form only in some members of bleeder families, especially amongst the women, whose menstruation is said by some to be early and abundant.

Certain conditions, psychical and physical, appear to cause an aggravation of the hæmorrhagic diathesis, or even to be the predisposing or exciting causes of hæmorrhage. Firstly, psychical: anger and other depressing emotions seem able to cause bleeding, interstitial or superficial, as in Fournier's,[1] Martin's,[2] and two of Resal's[3] cases. One of Grandidier's patients, also, suffered from hæmorrhage when excited.[4] The influence of the depressing emotions in the generation of hæmophilia has been already spoken of.

Secondly, physical: and these causes are many. i. Difference between day and night. Wachsmuth,[5]

[1] Fournier, *Gaz. des Hôp.* 1851, No. 123, p. 494.

[2] Martin, *Jenaische Annalen f. Phys. u. Med.*, Jena, 1850, Bd. ii. p. 312. Quoted by Reinert, *Ueber Hämophilie*, Diss. Inaug. Gött. 1869. p. 23.

[3] Resal, *Quelques pages sur l'hémophylie*, Thèse de Paris, 1861, pp. 27 and 31.

[4] For instance, when in church: but this man was so subject to bleedings that, when he washed his face, he had to be careful not to handle his nose at all roughly lest an intractable hæmorrhage should come on (See Grandidier, *op. cit.* p. 31.)

[5] Wachsmuth, *op. cit.* p. 12.

Mutzenbecher,[1] and myself,[2] have noticed the appearance of hæmorrhage at night rather than by day. ii. Changes of weather. Krimer,[3] Bicking,[4] Vieli,[5] Mutzenbecher,[6] Resal,[7] and Elsässer[8] speak of the appearance of spontaneous hæmorrhages in cold damp weather. With Tardieu's[9] patient they were very common after all changes of weather, especially fogs and snow. Great heat and cold seem in some cases to precede the bleeding. On the other hand, Otte,[10] availing himself of the exact meteorological observations published in the *Preussische Medicinal-Zeitung*, has found little or no relation between the changes of weather and the state of the patient. The appearence of bleedings was in no way influenced by the state of the barometer. iii. The seasons. A large number of observers have noticed that the bleedings come on more commonly in autumn and spring, than at any other time. Lange says that the least number of bleedings occur in the summer months.[11] iv. The moon. Krimer,[12]

[1] Mutzenbecher, quoted by Grandidier, *op. cit.* p. 97. The children would go to bed apparently well, and rise in the morning covered with ecchymoses. This plainly, however, allows of other explanation.

[2] See the case of James Day, p. 11.

[3] Krimer, reported by Nasse, Horn's *Archiv*, 1820, Mai-Juni, p. 418.

[4] Bicking, Hufeland's *Journal*, Bd. lxxxiv. Stück iv. p. 111.

[5] Vieli, reported by Grandidier, *op. cit.* p. 19.

[6] Mutzenbecher, quoted by Grandidier, *op. cit.* p. 96.

[7] Resal, *op. cit.* p. 18.

[8] Elsässer, Hufeland's *Journal*, Bd. lviii. Stück ii. p. 98.

[9] Tardieu, *Arch. gén. de Méd.* 1841, février, p. 187.

[10] Otte, *Ueber die Bluterkrankheit*, 1865, Leipzig, p. 31. More observations of this exact kind are wanted.

[11] Lange, *op. cit.* p. 194.

[12] Krimer, *op. cit.* pp. 412 and 420.

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and one or two observers after him, have fancied that they detected a relation between the increase of the moon, and the appearance of hæmorrhages. v. The use of wine. Dequevauviller noticed hæmorrhage to follow the use of wine, whenever the patient took it.[1] vi. Some have thought that the disposition to bleed is greatly aggravated after the first traumatic hæmorrhage.

The symptoms of hæmophilia may be considered under three heads: the bleedings, whether traumatic or spontaneous; the ecchymoses and petechiæ; the peculiar joint affections.

I. The bleedings are very common, occurring upon the slightest, or no, apparent cause, sometimes lasting for days or weeks: they are often extremely profuse, and most difficult to arrest.

i. Spontaneous bleedings. These are sometimes preceded by prodromata; sometimes not: and this variability occurs in the same individual at different times. They are uncommon in the second degree of the disease. The prodromata occur from 3 to 4 days before the onset of the hæmorrhage. There are signs of great plethora: the face full; the lips swollen and red; the ears red and hot; a frequent full pulse; beatings of the heart and carotids; dyspnœa; the skin hot to hand; headache and giddiness; the urine scanty and high-coloured, and the bowels confined. Sometimes there are darting pains in the limbs. There are often symp-

[1] Dequevauviller, *De la disposition aux hémorrhagies,* Thèse de Paris, 1844, No. 87, p. 36.

toms which indicate the part which is about to bleed; such as a pain in the back when hæmaturia is coming on; or an itching in the nasal cavity before epistaxis.[1] Wachsmuth[2] points out the psychical prodromata, and says they differ in the child and the adult. In the child there is usually great cheerfulness and liveliness; occasionally the reverse, listlessness; the child is very talkative, and inclined to a laughter which has something spasmodic in it. It is easily made angry, and then often bursts into violent crying; and it is easily frightened. In one case, epileptiform convulsions have been seen.[3] There is increased sensibility of hearing and sight. In the adult, there is a certain amount of good temper, accompanied by a marked restlessness. There is great sensibility which readily passes into angry ebullitions. The person becomes timid, and the speech quick. There is an increase in the sexual appetite. All these symptoms disappear within a short time after the setting in of the hæmorrhage. CHAP. IV.

I have never been fortunate enough, in the cases which have come under my notice, to see the prodromata described above. It would be interesting to compare the temperature of those parts, the cheeks, the ear, which feel so warm to the hand, with the temperature of the axilla or rectum: it might be well also to

[1] Otte has noticed a great hunger to come on a few hours before the occurrence of epistaxis (*Ueber die Bluterkrankheit*, p. 4.)

[2] Wachsmuth, *op. cit.* p. 15. The description seems to be based chiefly upon observations made in his own family, so that they must not be too hastily generalised.

[3] Beier, *De Haemophilia*, Diss. Inaug. Berol. 1864. p. 26.

CHAP. IV. note the state of the pupils, and the increase or diminution of the salivary secretion. According to Wachsmuth, an increase of this secretion is not uncommon before a bleeding from the mouth.[1] After these prodromata have lasted from 3 to 4 days, or, in those cases in which prodromata are absent, without any warning, the bleeding begins. These spontaneous bleedings come most commonly from the mucous membranes, very rarely from the skin, serous membranes, or within the cranium. The reason of this is obvious; the vessels of the mucous membranes are less supported than those of other parts.

In childhood, these persons more frequently bleed from the nose than from any other part. Few of them live to any age without suffering from it; and it apparently occurs indifferently out of either nostril. The next most frequent place of bleeding is the mouth: and in the mouth, the gums are the most predisposed to bleed; indeed some of these patients are unable to clean their teeth with an ordinary tooth-brush without drawing blood. The entire mucous membrane of the mouth may supply the blood; or only a part, as the lips and cheeks. A loose rough tooth will often cause bleeding. Bleeding from the gums usually occurs at the time of the first or second dentition.

After puberty, bleeding from the nose and mouth becomes less common, and is replaced very often by hæmaturia, or by bleedings from the bowel. Vomiting of blood and hæmoptysis become more common. It is less usual to have spontaneous bleedings from the

[1] Wachsmuth, *op. cit.* p. 15.

genital organs, male or female; and very rare from the ears or caruncle of the eye, from the ends of the fingers or hairy scalp, or into the serous cavities.

Grandidier gives the following numbers of local bleedings in 256 cases:[1] from the nose, 122; from the mouth, 34; from the stomach, 11; from the bowel, 33; from the urethra, 13; from the lungs, 15; from the end of the fingers, 4; from a swollen place on the scalp, 4; from the tongue, 4; from the ear, 3; from the eye-lids, 1; from the female genital organs, 10.

The amount of blood lost from these spontaneous bleedings varies very greatly: it may be but a few ounces, or it may be so great that the patient shall die. The spontaneous bleeding most commonly fatal is epistaxis; less frequently, bleeding from the mouth, bowel, or lung. There is only one case on record of death from hæmaturia.[2]

Resal has pointed out two forms of spontaneous hæmorrhage, which are, however, best marked in the second degree of this disease. In one, the hæmorrhages are small in quantity, but frequently repeated; they occur without prodromata, and always from the same mucous surface; they produce no constitutional effect. In the other form, there are often prodromata lasting three or four days, and the hæmorrhage is great in quantity, and has little tendency to be arrested spontaneously.[3]

[1] Grandidier, Schmidt's *Jahrbücher*, Bd. cxvii. p. 332.

[2] A case of Vieli's, a boy 8 years old (Grandidier, *op. cit.* p. 27).

[3] Resal, *Quelques pages sur l'hémophylie*, Thèse de Paris, 1861, No. 150, p. 48.

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It sometimes happens that when one hæmorrhage ceases, another comes on, until at last the patient dies exhausted. Or the same hæmorrhage may continue, with varying intermissions, until the death of the patient. The spontaneous bleedings sometimes alternate with the swellings of the joints.

ii. Traumatic bleedings. In some cases of hæmophilia, especially when the patients belong to the female sex, excessive bleeding does not take place when a part is wounded. And in some bleeders a wound will at one time be followed by bleeding that scarcely exceeds what is natural; at another, the same kind of wound will cause a hæmorrhage that cannot be checked. All vascular parts of the body may bleed furiously when injured, but the bleedings seem to be particularly dangerous when ecchymoses or hæmatomata are wounded. The smallest hurt is often sufficient to set life in danger;[1] a prick, a scratch, or cut, which another person would scarcely know had been inflicted. Death from bleeding has occurred after such slight wounds as the division of the frænum of the tongue,[2] the scarifications necessary

[1] The circumstances of one or two of the most striking cases may be here mentioned. A student, aged 22, received in a duel a cut on the face, 2 inches long, and 3 lines deep. Notwithstanding the use of every conceivable styptic, he bled continuously, and died on the 4th day. (Escherich, Henke's *Zeitschrift für die Staatsarzneikunde*, 1847, Bd. liii. p. 18.) A lad, aged 20, had an apple fall upon his nose: thereupon bleeding that could not be stopped, and death in 24 hours. The brother of this boy, being bled for pleurisy, died of hæmorrhage from the incision, consequent gangrene of the arm, and amputation. (Donkersloot, *Nederlandsch Lancet*, 1850, p. 419.)

[2] Rieken, *Neue Untersuchungen*

for vaccination,[1] the application of leeches, or the extraction of a tooth. This last is an especially common cause of death, and ought never to be undertaken in a patient with this disposition.

But these patients differ very much in the amount of handling that they will bear. In one family, venesection may be done, or cupping glasses applied, without much difficulty in stopping the bleeding: while in another, even the application of blisters may be in the highest degree dangerous. I have seen a tooth drawn without any remarkable hæmorrhage: few operations are more dangerous. A small superficial hurt, especially if torn or lacerated, is thought by some[2] to be more dangerous than a deep clean-cut wound. Wachsmuth says that the proportion of dangerous bleedings, caused by blunt instruments, is to those caused by sharp instruments, as 5 : 1.[3] It must not be forgotten, however, that, in nearly all the cases of surgical interference for the arrest of the hæmorrhage, the wound made by the knife has bled as furiously as the original injury.[4] The

in Betreff der erblichen Neigung zu tödtlichen Blutungen, Frankfurt a. M. 1829. p. 14.

Wardrop, *On Blood-letting*, London, 1835, p. 18. Three cases reported by Ward.

1 Henschel, reported by Grandidier, Schmidt's *Jahrbücher*, Bd. cxvii. p. 331.

2 Wachsmuth, *op. cit.* p. 23; and Allan, *Monthly Journal*, 1842, pp. 501 and 503. Fordyce is frequently quoted in support of this statement: but there is nothing whatever in his description (*Fragmenta chirurgica et medica*, p. 41) which warrants such an assertion.

3 Wachsmuth, *loc. cit.*

4 Lafargue, *Revue Méd.* 1835, t. iv. p. 92.

Lebert, *Arch. gén. de Méd.*, 1837. sept. p. 40.

Thal, Kleinert's *Repertorium*, 1831, Mai, p. 123.

CHAP. IV. explanation of these two contending statements probably lies in the fact that the disposition to hæmorrhage varies so greatly at different times in the same person; that a wound, whether clean-cut, or otherwise, may be made at one time without much risk; whilst at another, when the disposition to bleed is at its highest, the very means that the surgeon uses to stop the bleeding elsewhere, become a fresh source of loss of blood.

Vaccination, as a rule, may be done with safety: there is only one case on record, in which it is even doubtful if the child were the subject of hæmophilia,[1] in which death has followed this small operation. There is also another case in which dangerous bleeding followed the insertion of the vaccine matter into 4 punctures:[2] nevertheless, the vaccination succeeded. Rieken[3] seems to think that the vaccination of a bleeding part might be useful in stopping the hæmorrhage. Be this as it may, in all the other cases where the fact is noticed at all, it is said that the vaccination ran its usual course.

Hughes has described a family in whom the application of blisters "drew blood instead of water;"[4] and says that he has seen death occur twice from this cause.

[1] A little girl aged 3 months, suffering from whooping-cough, among whose relations no account of a disposition to bleed could be obtained, died in a few days after vaccination, of bleeding, not only from the scarifications, but also from a place on the nose which the child had scratched. (Henschel, Schmidt's *Jahrbücher*. Bd. cxvii. p. 331.)

[2] Heyfelder, *Medicinische Zeitung (Vereins)*, Berlin, 1833, p. 216.

[3] Rieken, *op. cit.* p. 116.

[4] Hughes, *American Journal of Medical Science*, 1833, vol. xi. p. 542.

Usually, however, blisters are followed by no bad result, even when suppuration is set up. CHAP. IV.

If abscesses be opened, either by the surgeon or of themselves, a profuse bleeding usually takes place. Still more profuse is the bleeding when a blood tumour or extravasation of blood is wounded, and the hæmorrhage is only to be stopped with great difficulty.

Those wounds which are not attended by great hæmorrhage usually present nothing unusual: those, however, which bleed so greatly, rarely heal by the first intention. They very often suppurate; and sloughing is not uncommon. When the wound begins to suppurate, the hæmorrhage usually stops: but even then the patient is not secure; for after the wound has apparently healed, the bleeding may burst out again after a few days: and this alternation of healing and bleeding may go on for several weeks.

The bleeding, whether spontaneous or traumatic, is almost always capillary. The blood oozes out of the part continuously, without any distinct rise or fall: no bleeding points can be seen, but the blood trickles out as if pressed from a sponge. In Blagden's case, a bleeding artery was seen and secured; but the vessel, from the thinness of its coats, soon gave way.[1] In the cases where amputation has been done, or the vessel tied in its length, there is no mention of any difficulty in securing the arteries.[2]

[1] Blagden, *Med.-Chir. Trans.*, vol. viii. p. 225. An artery on the forehead was bleeding. Some years after, Sir B. Brodie tied the carotid in an attempt to stop the bleeding after the taking out of a tooth.

[2] Clutterbuck, *Lancet*, 1826,

CHAP. III.

A bleeding may last only a few hours, or for 18 weeks.[1] In the first instance, the loss of blood in so short a time may be so great, that the patient shall lie as if dead, be pulseless, and blanched. The shortest time on record, between the first occurrence of fatal bleeding and death, is six hours; a boy aged 3 was cut for the stone in Guy's Hospital about 2 o'clock in the afternoon, and died the same night at half-past 8.[2] Epistaxis has proved fatal in 24 hours,[3] and a bite of the tongue in an infant in 36 hours.[4]

Very commonly profuse bleeding does not immediately follow the infliction of the wound; but the bleeding comes on a few hours, or it may be a day or two, after the hurt has been given.

The quantity of blood lost in a very short time may be enormous; but this rapid loss of blood does not seem

April, p. 99. A limb was amputated, and the patient died of the continuous oozing from the stump.

Lebert, *Arch. gén. de Méd.*, 1837, sept. p. 40. The radial and brachial arteries were tied.

Donkersloot, *Nederlandsch Lancet*, 1850, p. 419. Amputation of the arm was done for gangrene following the incision for phlebotomy.

Lafargue, *Revue méd.*, 1835, t. iv. p. 92. The crural artery was tied.

Wilmot, *Dublin Journal of Med. Science*, 1841, vol. xix. p. 234. The lingual artery was divided by a cut, and tied after the hæmorrhage had lasted for two days.

Sentex, *Mémoires de la Soc. méd.-chir. de Bordeaux*, 1866. t. i. p. 311. The brachial was tied for a crush of the forearm.

[1] Uhde, *Deutsche Klinik*, 1850, p. 540. This man usually bled for three or four weeks after any trifling accident.

[2] Durham, *Guy's Hospital Reports*, 1868, vol. xiii. p. 490.

[3] Donkersloot, *loc. cit.*

[4] Theinhardt, reported by Nasse, Horn's *Archiv*, 1824, Juli-August, p. 121.

to be so dangerous as longer continued, frequently recurring, smaller bleedings. Schäfer's patient lost by spontaneous bleeding from the mouth, chiefly the gums, three or four pounds of blood in 24 hours:[1] one of Krimer's lost, after the taking out of a tooth, three and a half pounds in the same time.[2] The medical student, whose case has been recorded by Coates, also had a tooth taken out, and in less than 24 hours, half a gallon of blood had been poured out: the bleeding lasted 10 days, and the entire quantity of blood lost was estimated at not less than three gallons.[3] In the younger Thore's case of a boy of 5 years old, nearly a pound of blood was lost on two occasions from a very small wound.[4] In Miller's case, 5 or 6 pounds of blood were lost in 36 hours from the gums.[5]

Liston was the first to make observations on the composition of the blood in this disease.[6] After asserting that it was deficient in fibrin, and that the globules were broken down or diffluent, he says "the blood was altogether in a bad state, containing a proportion of globules with all the characters of those entering into the composition of pus."[7] But leaving these, and similar

[1] Schäfer, *Medizin. Zeitung* (*Vereins*), Berlin, 1836, p. 130.

[2] Krimer, reported by Nasse, Horn's *Archiv*, 1820, Mai-Juin, p. 416.

[3] Reynell Coates, *North American Medical and Surgical Journal*, Philadelphia, 1828, vol. vi. p. 45.

[4] Thore, *Gaz. méd. de Paris*, 1856, p. 653.

[5] Miller, *Edinburgh Medical Journal*, 1856, Jan. p. 638.

[6] Nasse, as well as Meckel, had previously directed attention to the state of the blood. (Reil's *Arch. f. d. Phys.*, 1811, p. 266; and *Deutsches Arch. f. d. Phys.* 1816, Bd. ii. p. 138.)

[7] Liston, *Lancet*, 1839, April, p. 137.

CHAP. IV. inexact observations,[1] the attempts at chemical analysis will present more interest. At the very outset a considerable difficulty presents itself: our knowledge of the chemical composition of the blood, even at the present day, is not so perfect that much light can be expected to be thrown upon the pathology of hæmophilia by the help of chemistry. The older analyses differ among themselves: in Heyland's analysis the blood contained a considerable excess of fibrin, 5 per mille.[2] In Wachsmuth's case, nothing unnatural could be discovered:[3] while in Tardieu's case, the blood was found to be deficient in fibrin and cruor; its density much diminished; and six hours after the blood was drawn, it had not coagulated.[4] But the examination does not seem to have been very carefully made.

Analyses of the blood in hæmophilia have been made within the last 10 years by three observers. There is an analysis by Ritter, reported by Gavoy,[5] of the blood

[1] Such as Rogers' statement, reported by Otto (*Medical Repository*, New York, 1803, vol. vi. p. 1.) that the blood "seemed to be in a high state of effervesence."

[2] Heyland, quoted by Lange, *op. cit.* p. 198. The analysis is: 780 of water, 5 of fibrin, 70 of albumen, and 137 of cruor, in 1000.

[3] Wachsmuth, *op. cit.* p. 16. The analysis was made by Dr. Duflos of Breslau: an ounce of blood from the nose was examined.

[4] Tardieu, *Arch. gén. de Méd.* 1841. févr. p. 190. He does not give numbers: the blood was furnished by the operation of phlebotomy, which was conducted 8 days after a bleeding from the gums had ceased, which bleeding lasted 4 days. Another analysis, made six months afterwards, confirmed the results of the former.

[5] Quoted by de Fleury, *Mém. de la Soc. méd.-chir. de Bordeaux*, 1866, t. i. p. 306. I regret very much that I have been unable to procure Gavoy's original publica-

of a boy, aged 14, who died in a hospital at Strasburg. There was found:

Water	92·320
Fibrin	·264
Albumen	7·390
Salts	·026

In the second analysis:

Water	92·244
Fibrin	·264
Albumen	7·470
Salts	·022

Otte, following Scherer's method, analysed the blood of his patient; nearly a pound of blood was lost in 5 hours from the nose; no hæmorrhage having taken place for 15 days before; nothing unusual was noticed about the coagulation. The specific gravity of the serum was 1·029. The estimation gave the following results:[1]

Water	905·04
Albumen	79·54
Fibrin	4·35
Fat	1·82
Soluble Salts	5·43
Extractives	3·82

Leconte analysed some blood, furnished by an epistaxis, from a woman suffering from the second degree

tion. It would seem that the blood analysed was lost from the nose.

[1] Richard Otte, *Ueber die Bluterkrankheit*, Leipzig, 1865, p. 23.

CHAP. III. of hæmophilia.[1] The coagulum was well formed and resistant, the serum properly separated and limpid, and the corpuscles showed no alteration under the microscope. The blood contained 14·1464 per cent. of dry residue, which consisted of:

Fibrin	·1654
Albumen	7·5080
Corpuscles	6·4730

A second analysis, not completed, made six months later, gave 14·540 per cent. of dry residue. In a few days, a third analysis was made and gave the following results:

Fibrin	·2000
Albumen	7·5000
Corpuscles	6·2590
Water	86·0410

It will be observed at once that these analyses have failed to discover any unnatural state of the blood. They were all, however, made without any attempt at a distinction of the constituents of the plasma and the corpuscles: and greater attention might have been paid to the amount of inorganic salts. It is very probable, however, that in nearly all cases, no chemical alteration of the blood would be discovered.

Most of the earlier writers state that the blood does not coagulate. According to recent observations, the truth seems to be that the blood at first coagulates naturally; but that after a great deal has been lost, it coagulates feebly, or not at all. The blood is then so thin that it resembles water in which fresh meat has been washed, and scarcely stains linen. Chemical

[1] Leconte, reported by Resal, *Quelques pages sur l'hémophylie*, Thèse de Paris, 1861, p. 56.

examination of the blood in this state seems to be quite wanting.

It is somewhat surprising, considering the ease with which microscopical examinations of the blood corpuscles can be made, that so few should be at present recorded. Uhde,[1] Finger,[2] and Resal[3] found nothing unnatural in the shape or appearance of the corpuscles: Finger, however, thinks that there was an undoubted increase in the relative number of the red corpuscles in about 4 or 6 days after the beginning of the bleeding, together with a complete disappearance of the colourless corpuscles: when the bleeding had lasted a longer time, the blood becoming less red, and the coagulum less firm, there was a decrease of the red, and a slight increase of the white, corpuscles. Dr. Moxon found after death an increase of the white corpuscles, when the bleeding had lasted only six and a half hours.[4] In Tardieu's[5] case, the corpuscles were regular in shape, but the nucleus (*sic*) was pale, transparent, and ill-formed.

The few facts at our command seem to point to no unnatural state of the blood in hæmophilia; the changes, which take place in the blood after successive bleedings have occurred, are probably due to the rapid loss of the

[1] Uhde, *loc. cit.*

[2] Finger, Schmidt's *Jahrbücher*, Bd. cxvii. p. 330.

[3] Resal, *loc. cit.*

[4] Durham, *loc. cit.* An increase in the amount of white corpuscles is usually observed after hæmorrhage. Schünemann (*Arch. f. path. Anat.* Bd. xli. p. 289.) found the blood, after death from long-continued bleeding from the socket of a tooth in a young man of 21, to be watery and to contain fewer red corpuscles: but he makes no mention of the white corpuscles.

[5] Tardieu, *loc. cit.*

fluid, and can scarcely be ascribed to the disease. Chemistry and the microscope have hitherto done but little in the discovery of morbid states of the blood in other diseases attended with a hæmorrhagic diathesis, as scurvy and purpura; and it seems unlikely that they will prove of much assistance until our knowledge of the natural composition of the blood have been much enlarged.

The prodromata which have been spoken of above as preceding the spontaneous bleedings, are continued for a short time after the hæmorrhage has begun; but when the plethora of the vascular system has relieved itself, these symptoms, as might be expected, disappear.

The bleeding, spontaneous or traumatic, when excessive, can seldom be at once checked by any means hitherto recommended. Sometimes the bleeding does not cease until the patient faint; and even then there is a danger of a renewal of the hæmorrhage on the return of consciousness. Either after one profuse hæmorrhage, or, as is more common, after a series of bleedings, interrupted by short intervals, all the symptoms of true anæmia show themselves. The pulse becomes rapid, small, and compressible: if the bleeding have been great, it may not be felt at all, and the impulse of the heart may become scarcely perceptible. There is a murmur with the first sound at the base, prolonged iuto the great arteries, and the venous hum in the veins of the neck. The face becomes blanched, almost transparent, like a piece of bleached wax: this appearance is very noticeable in the ears and tongue, and is so peculiar, that those who have once witnessed it, cannot fail to have been struck by the sight.

Should the bleeding continue, the pulse, and impulse of the heart, can no longer be perceived; the blood which flows resembles coloured serum or bloody water rather than blood; delirium and hallucinations, or exaltations of the special senses with retention of consciousness, follow; and general convulsions usher in the fatal termination. CHAP. IV.

Should, however, the result be favourable, the patient lies long, as in a deep sleep; and awakes to suffer from a most profound anæmia. When the blood from the nose or mouth has been swallowed, a gastro-intestinal catarrh is often set up; or coagula of blood in the intestine may cause great pain and trouble in passing. The same difficulty may arise after extreme hæmaturia, though this form of bleeding seldom causes danger to life.

The blood lost is only very gradually regained. The patients look anæmic for four or six months after a great bleeding. The statement that they quickly pull up again is not correct.

In a few cases, depraved appetite, like that shown by chlorotic women, has been observed. The two brothers Buel noticed this in two boys in the same family, after hæmorrhage: one had a tendency to eat sand; the other, common earth.[1] Gintrac also speaks of the avidity with which one of his patients swallowed small pieces of stone;[2] he had thus destroyed the wall against which his bed was placed. In the last half year of the life of one of Elsässer's patients, aged 3, he showed a disposi-

[1] W. and S. Buel, *London Medical and Physical Journal*, 1818, vol. xl. p. 430.

[2] Gintrac, *Cours théorique et clinique de Pathologie*, Paris, 1853, t. iii. p. 110.

CHAP. IV. tion to swallow sand and spice, even directly after meals. After bleedings, he liked cold food.[1] Wilmot's patient, a boy aged six, showed a strange desire to eat clay and lime, and his bowels were generally very irregular.[2]

II. The petechiæ and ecchymoses of hæmophilia represent an interstitial form of hæmorrhage; like the external bleedings, they may be either spontaneous or traumatic.

i. In those cases where they are present, spontaneous ecchymoses are often the first signs of the disease. With some exceptions, they usually appear in the first year of life; but their presence is not so constant as the external bleedings. They are mostly situated in the connective tissue under the skin: at least, this is the place where they are most commonly seen; for no means exist by which, during life, their presence in the connective tissue of internal organs, such as the pericardium or pleura, can be ascertained.[3] Wachsmuth says that they are most common on the external parts of generation, and on the buttocks in infants.[4] Lange agrees with this,[5] and adds that the face usually escapes. The spontaneous ecchymoses vary in size, being usually small, from a pin's point or head, which is common, to a halfpenny; larger than this have not been seen.

[1] Elsässer, Hufeland's *Journal*, 1824, Bd. lviii. Stück ii. p. 99.

[2] Wilmot, *Dublin Journal of Medical Science*, 1841, vol. xix. p. 239.

[3] Small ecchymoses under the serous membranes are not uncommon in other diseases where a hæmorrhagic diathesis is present.

[4] Wachsmuth, *op. cit.*, p. 25.

[5] Lange, *op. cit.*, p. 215.

It is not at all rare to meet with cases of hæmophilia in which the spontaneous ecchymoses are altogether absent. And, on the other hand, the ecchymoses sometimes occur when the external bleedings are absent; they then represent a less intense form of the disease, common amongst the near relations of bleeders, especially the women. CHAP. IV.

The appearance of these ecchymoses does not seem to depend upon any time of day or season of the year; sometimes they alternate with external bleedings or swellings of the joints, or are the forerunners of hæmorrhage.

ii. The traumatic ecchymoses are caused by external force, usually injuries or blows which would produce no such effect in a healthy person.[1] They are, according to Wachsmuth, rare on the trunk; he says that they are most common on parts removed from the heart, such as the head and face, nates and extremities; their favourite situation is the hairy scalp.[2]

A slight degree of this tendency to traumatic ecchymosis is by no means uncommon in delicate women. These ecchymoses are usually larger than the spontaneous; in fact there is no limit to the extent that

[1] In Allan's case, (*Monthly Journal*, 1842, June, p. 503) the occupation of the lad was a writer, and the left arm was black from the elbow to the wrist from pressure upon the desk; also a black line across the belly from the same cause. In Lafargue's case (*Revue médicale*, 1835, p. 91) a little girl struck a bleeder, aged 41, with her elbow upon the lower part of the arm: thereupon the arm swelled enormously with blood up to the axilla.

[2] Wachsmuth, *loc. cit.*

CHAP. IV. they may attain: they may fill the connective tissue of a limb with blood;[1] or more, cause death by hæmorrhage into the connective tissue generally.[2]

The spontaneous ecchymosis is often preceded by the symptoms of congestion and plethora, with pains in the limbs, which have been described above as the prodromata of the spontaneous external bleedings. When formed, the ecchymoses do not differ from those seen in other diseases attended by a hæmorrhagic diathesis, or from those which are the result of bruises. They are of a deep purple or reddish blue colour; and when disappearing, they show the usual play of colours, green and yellow, which attend the absorption of effused blood. Sometimes they are painful; at other times not, even upon pressure. If they should be opened by accident, bleedings most alarming and difficult to stop almost invariably follow.[3]

In connection with the traumatic ecchymoses must be mentioned the so-called blood tumours. These are to be distinguished from the extravasations of blood into the connective tissue generally of a limb, just as an œdema is to be separated from a collection of fluid in a

[1] Sir William Jenner used to mention, in his lectures, a case in which the fall of an india rubber air ball upon the thigh had filled the connective tissue of the limb with blood from the knee to the trochanters.

[2] Mutzenbecher (quoted by Grandidier, *op. cit.* p. 72.) records a case where a child, whose age is not stated, died in consequence of the bleeding into the connective tissue, following a fall upon the chest.

[3] In a case spoken of by Wilmot (*Dublin Journal of Medical Science*, 1841, vol. xix. p. 237.) death occurred from the hæmorrhage following the opening of an ecchymosis.

cyst. It has been stated by a writer,[1] who has had large opportunities for observations, that the blood tumours sometimes arise spontaneously; and, by another, as a consequence of mental emotion:[2] but it seems very probable that in the instances mentioned they were due to some slight injury that had been forgotten. In the great majority of cases, a blow or injury precedes their appearance: and a slight injury may cause a large tumour.[3]

The size of the tumours may reach to that of an adult's head.[4] The skin over them is black or black blue, surrounded by a zone of red. The temperature to the hand is sometimes raised, and the surface is usually tender. The tumours disappear slowly, with the usual play of colours. They very rarely suppurate. Rieken[5] felt within one of these tumours an inelastic solid body; and Hopf,[6] on opening a similar tumour in

[1] Vieli, quoted by Grandidier, *op. cit.* p. 70.

[2] Fournier, *Gaz. des Hôp.* 1851, No. 123, p. 494.

[3] A man, aged 41, fell against the key of a door: soon after, a tumour formed on the right side of the abdominal walls, beginning at the level of the 11th rib, and extending to the superior iliac spine; it was six inches long, three broad, and two high. (Lafargue, *Revue médicale*, 1835, p. 89.)

[4] Thormann, Gräfe und Walther's *Journal der Chirurgie*, 1840, Bd. xxx. p. 298. Three days after a blow from the foot of a cow, a swelling as large as a man's head appeared in the scrotum of a bleeder, aged 23. Also Vieli (reported by Grandidier, *op. cit.* p. 23) describes an enormous blood tumour in upper part of right thigh.

[5] Rieken, *Neue Untersuchungen in Betreff der erblichen Neigung zu tödtlichen Blutungen*, Frankfurt a.M. 1829, p. 28.

[6] Hopf, quoted by Grandidier, *op. cit.* p. 71. The tumour resembled a gouty deposit and was opened by caustic; about 24-30 ounces of a brown red fluid es-

CHAP. IV. a bleeder aged 50, found concretions not unlike gall-stones. Coagula of blood not unfrequently become calcified; a familiar example of this is seen in the phleboliths so commonly found in the pelvic veins, having their origin in the calcification of thrombi.

III. The subjects of hæmophilia are prone to an affection which is oftentimes far more distressing and vexatious than the attacks of hæmorrhage. The joints, especially the larger joints, have a disposition to become painful, swollen, and filled with fluid. This disorder is continually recurring, so that some patients are scarcely ever free from it, and they are cripples for the greater part of their life.[1] The large joints are those most commonly attacked, the knee being the joint which suffers most; the ankle, elbow, shoulder, and hip being seized upon more rarely, and, in the same patient, at longer intervals. The joints of the wrist, and of the fingers and toes are but seldom swollen.

The joint affected becomes swollen, often suddenly. Sometimes the swelling attains a great size, and the knee of a child may become as large as an adult's head. The swelling is attended by great pain, which increases towards evening; and by fever, which may be so great that the thermometer in the axilla may rise to 104° or 105°F. The skin over the swelling is warm to the hand, but never reddened; it is much stretched, and

caped, of the consistence of a thin syrup, very like that of the pulp of tamarinds, and mixed with black red, shining, polished concretions, looking like gall-stones. The tumour continued to discharge, the fluid at the end resembling coffee grounds, until the patient's death from collapse.

[1] As in the cases of Bickell and Robins, pp. 3 and 14.

some observers have from this circumstance described the swelling as hard. It has rather a soft, somewhat fluctuating feel, and the ends of the bones forming the joint can rarely be felt. Movement, as a rule, increases the pain; sometimes, however, passive motion may be borne. The length of time which the swelling lasts is very uncertain: as a rule it lasts longer in the larger joints. Sometimes it disappears in a few days; or lasts many weeks or months. It may disappear in one joint, only to reappear in another; or the swellings of the joints may alternate with hæmaturia, or some other form of hæmorrhage.[1] When the swelling is gone, the joint may completely recover, or the ends of the bones may be enlarged, and more or less permanent impairment of motion may be left.

There is always a great liability to recurrence of the disease in the affected joint, and during convalescence there is always great risk of a relapse.

The causes of the swelling may be either traumatic or idiopathic. The traumatic origin of the swelling has been denied.[2] But I think I have seen cases where such a source seemed to be the only possible one. The patients have been in excellent health, the weather has been mild or warm, a blow or other injury has been received, and in 24 hours the joint injured has been swollen and painful. There is, also, often a black or blue spot of extravasated blood near the joint. These

[1] Otto Weber, v. Pitha u. Billroth's *Handb. d. Chirurgie*, 1865, Bd. i. Abth. i. Lief. i. p. 129. Gröschner (Rust's *Magazin*, Bd. xxxvi. p. 397) relates two cases where the pain in the knee was suddenly relieved by an abundant bleeding from the nose.

[2] Lange, *op. cit.* p. 211.

CHAP. IV. circumstances point very clearly to the possibility of a traumatic origin of the swelling. On the other hand, there can be no doubt that the most common cause of the swellings is exposure to cold, or the occurrence of cold damp weather. Thus they are most frequently seen at the beginning of the spring, or end of the autumn. Sudden changes of weather, as from frost to thaw, have a great influence in producing them.

Allied clinically, and probably also pathologically, to the swellings of the joints, are the pains felt in the limbs, especially about the joints. These pains are often so severe that they disturb the function of the limb, making the patient walk with difficulty. The pains are sharp[1] and usually increased towards night, and, like the swellings of the joints, often follow exposure to cold and damp, especially in the spring and autumn: in like manner they may also alternate with the spontaneous interstitial or superficial hæmorrhages; or the pains may form part of the prodromata of hæmorrhage.

[1] In some of Vieli's cases, these pains set in with great violence and suddenness, and the patients were so weakened thereby that they had to keep their bed: the pains usually lasted about 9 days; and then left the knee or ankle, swollen, and blue. See Grandidier, *op. cit.* p. 73.

CHAPTER. V.

IDIOSYNCRASIES OF HÆMOPHILIA.

In the last chapter, the ordinary symytoms of hæmophilia were discussed. It is now proposed to speak of the peculiarities which the disease exhibits, either in its own progress, or in influencing the occurrence and progress of other diseases.

Murmurs over the heart and great vessels have been noticed by several observers: they are such murmurs as are caused by a poor and watery state of blood. An increased and diffused impulse of the heart has also been several times recorded.[1] These phænomena about the heart have nothing to do with the pathology of hæmophilia: they are due solely to the condition of blood.

In four cases, already mentioned,[2] there has been, after hæmorrhages, a depraved appetite for clay, sand, earth, &c., similar to the pica of chlorotic and pregnant women.

Some authors mention a great sensibility to cold, especially to damp cold: this tendency was shown in its highest degree in a family described by Bicking. In dry weather, the father was quite well, but he feared the cold as an unavoidable source of illness. The son was a perfect hygrometer.[3]

[1] Grandidier *op. cit.* p. 82.

[2] See p. 65.

[3] Bicking, Hufeland's *Journal*, Bd. lxxxiv. Stück iv. p. 111.

CHAP. V. In some few cases, hæmorrhages have followed the use of mercury. Burnes[1] found that on taking blue pill, profuse hæmorrhages from the gums and nose occurred; and this symptom returned again when the blue pill was repeated. Bicking[2] found that calomel was ill borne in the family under his observation; it once caused bloody stools and vomiting. Elsässer[3] noticed vomiting and two bloody stools after the prescription of a powder containing calomel, magnesia, and jalap. In the great majority of cases, however, the preparations of mercury do no harm whatever. Wachsmuth[4] thinks that mercurial ointments make the swellings of the joints more obstinate: but no other observer has noticed the same mishap.

Hæmophilia influences very slightly, if at all, the occurrence and progress of other diseases. The American physicians enjoyed the advantage of observing families of these patients; and they say that the diseases, to which they are subject, differ in no way in their course and character from those of other individuals. Like other children, they pass through measles, scarlet fever, and whooping cough, without anything remarkable; and later in life, should they chance to suffer from acute disease, there is nothing characteristic either in the course or mode of recovery. They seem, however, rather more liable to acute affections within the chest, such as pneumonia and pleurisy, than to any other form of acute disease. And in some of these cases, there is a tendency, during the course of the disease,

[1] Burnes, *Lancet*, 1840, Dec. p. 405.

[2] Bicking, *op. cit.* p. 112.

[3] Elsässer, Hufeland's *Journal*, Bd. lviii. Stück ii. p. 103.

[4] Wachsmuth, *op. cit.* p. 29.

to hæmorrhages, whether from the nose, which is the more common, or from the urinary organs. Catarrhs, influenza, croup, rheumatism, peritonitis, orchitis and erysipelas have been observed among them, each running its usual course. CHAP. V.

Among chronic diseases, rheumatism and 'scrofula' are mentioned most frequently. Vieli, in his great experience of the large families at Tenna, says that, after hæmorrhage, dropsy and gangrene are the most common causes of death.[1] Gangrene is not an uncommon accident among the subjects of hæmophilia; Vieli says it is an ordinary result of a wound,[2] and twelve other writers speak of sloughing or gangrene following a traumatic hæmorrhage, or an injury.

Chronic skin diseases are seen amongst bleeders: chiefly forms of impetigo and 'pityriasis.'

Phthisis does occur amongst these patients and their families, but there is no apparent disposition to the disease. Convulsions are common when the loss of blood has been very great; but epilepsy has only been noticed 4 times: in one case, a hæmorrhagic cavity was found in the brain after death.[3] In another, con-

[1] Vieli, reported by Grandidier, *op. cit.* p. 19.

[2] Vieli, reported by Grandidier, *op. cit.* p. 18.

[3] In the case recorded by Cousins. (*Med. Times and Gazette*, 1869, vol. ii. p. 278) The other three cases are Gintrac's, where no *post mortem* examination was allowed; Beier's, and Otte's, where the boys were still alive at the time of publication. There must be great risk of an extravasation of blood within the cranium at each epileptic attack: practically this does not seem to exist; and there is also no record of ecchymoses in the face being noticed after the seizure, an accident not uncommon in some epileptics. Otte, indeed, noticed that, during the fit, ecchymoses did not follow bruises.

CHAP. V. vulsions seem to have preceded and attended the bleedings.[1]

True gout is extremely rare amongst the subjects of hæmophilia, as may readily enough be supposed from the age of the majority of the patients. Those cases which are called gout by the Germans are nothing more than the peculiar joint swelling.

In four of Rieken's patients there was a fœtid discharge from the ear: in one of them it almost disappeared after the use of cod liver oil.[2]

[1] Beier, *De Haemophilia*, Diss. Inaug. Berol., 1864, p. 27.

[2] Rieken, *Neue Untersuchungen u.s.w.*, passim.

CHAPTER VI.

Morbid Anatomy and Pathology of Hæmophilia.

The examination after death of persons who have suffered from hæmophilia has hitherto thrown but little light upon the disease. The number of such examinations is now very considerable; but careful and thorough examinations are still wanted. In the greater number of cases, it is stated that all the organs examined, especially the heart and vessels, were natural. The appearances of death after great loss of blood are present; the body is found emptied of blood, the skin and tissues extremely pale, the face and ears are semi-transparent, as if made of wax. The ecchymoses, if present during life, remain after death; they may be noticed in the mucous membranes and connective tissue. The rigor mortis is often so considerable that the body may seem to have gained several inches in length. Putridity quickly comes on. Such is the negative result of careful examinations made by Grandidier in three cases[1] Chap. VI.

[1] Grandidier, *op. cit.* pp. 30 and 151; and Schmidt's *Jahrbb.* Bd. xxviii. p. 170. The first-mentioned case was a boy of 13, whose pharynx was found to be changed into a red semi-fluid mass: the second was a child a few days old upon whom ritual circumcision had been done: the third was a boy in his third year; nothing unnatural was found beyond very thin coats to the stomach and intestines.

CHAP. VI. and by Lebert,[1] Elsässer,[2] Moxon,[3] Spahn,[4] Assmann,[5] and Resal,[6] in one case each. In a bleeder, aged 12, at whose examination after death I was present a few years ago, nothing was found but great bloodlessness of every part.

But although the bodies of bleeders show no constant anatomical change, yet certain alterations have been noticed with some degree of frequency: these are mostly an unusual thinness, or other disease, of the coats of the vessels; or some mal-formation of the heart. Under these two heads, nearly all the morbid appearances yet found may be classed.

Blagden was the first to notice an unusual thinness of the arteries. In a young man, aged 27, the coats of the temporal artery and some other branches of external corotid were nearly transparent; and they were thinner than usual. The texture of the carotid, which had been ligatured, was natural, but "there were several opaque white depositions on the outer surface of its inner coat, such as precede ossification."[7] But two years after, in 1819, James Wilson gave the following account of the

[1] Lebert, *Arch. gén. de méd.* 1837, sept. p. 40. No thrombus had formed above or below the ligatured points of the radial and brachial arteries; but the man seems to have died on the same day that the arteries were tied.

[2] Elsässer, Hufeland's *Journal*, Bd. lix. Stück iii. p. 111.

[3] Moxon, reported by Durham, *Guy's Hospital Reports*, 1868, vol. xiii. p. 491.

[4] Spahn, Schmidt's *Jahrbb.* Bd. cxxxix. p. 173. Small ecchymoses were found in the stomach.

[5] Assmann, *Die Hämophilie*, Diss. Inaug. Berol. 1869. p. 19. Both pleuræ were full of fluid.

[6] Resal, *Quelques pages sur l'hémophylie*, Thèse de Paris, 1861, p. 26.

[7] Blagden, *Med. Chir. Trans.* 1817, vol. viii. p. 227.

examination after death of a boy, between 3 and 4 years old, the subject of hæmophilia, and who bled to death after biting his tongue. "The whole of the viscera appeared to be perfectly healthy, but the aorta and every branch sent off from it seemed to resemble veins more than arteries; the coats were not more than one half of their usual thickness, they had not sufficient elasticity to preserve their cylindrical form in the dead body when deprived of blood; and even in the popliteal artery, notwithstanding there had been so much loss of blood, the artery did not appear to be contracted, nor were any muscular fibres to be discovered in its coats."[1] Hooper also found, in a bleeder 25 years old who injured his arm by a fall from his horse and bled to death therefrom, "numerous pellucid patches all over the artery (brachial) through which the probe could be seen, and the profunda superior and inferior and ramus anastomoticus presented similar appearances. There was an evident deficiency of the fibrous coat."[2] No further examination is reported. Fischer also found the walls of the arteries very thin, and their elastic coat transparent, in a bleeder aged 18, who died of the hæmorrhage following the extraction of the stump of a tooth.[3]

In a case recorded by Lemp, the *post mortem* examination was made by Professor Virchow; there was found some fatty degeneration of the fibres of the heart; and of the inner coat of the aorta, an appearance not very rare at the age of 24. The aorta was narrow, and the thy-

[1] James Wilson, *Lectures on the Blood, etc.*, London, 1819, p. 412.

[2] Hooper, reported by Burnes, *Lancet*, 1840, Dec. p. 405.

[3] Fischer, Schmidt's *Jahrbücher*, Bd. lxxxvii. p. 136.

CHAP. VI. mus persistent. No alteration could be detected in the small arteries or capillaries; nor in the nerves.[1]

[1] Lemp, *De haemophilia nonnulla*, Diss. Inaug. Berol. 1857, p. 17. Since, to use the words of this author, "hucusque sectio tanta diligentia et a tanto antistite non instituta," it may be desirable to give the chief part of the report of this examination, especially since the dissertation is rather difficult to procure.

"Vena cruralis omnibus locis amplissima, valvulae evidentes, verum tenues, tunica intima spissata, partim maculis conspersa. Arteriae pro ratione angustae, parietes satis spissi, elasticitas potissimum in diametro longitudinali permagna, tunica intima omnino sana, paucis locis nubila, obscura et albida.

"In cavo abdominis praeter parvam copiam transsudati cadaverosi nusquam adhaesio aut pigmentatio quaedam inventa est. . . In abdominis visceribus nulla mutatio notabilis detecta. . . . . In mediastino antico glandula thymus perstitit. . . . . . Pulmones parum hypostasi oppleti, ceterum sani. In sacco pleurae et pericardio exigua transudati cadaverosi copia. Cor nonnihil parvum, pallidum, in basi et ventriculo dextro satis large adiposum, in parte anteriore et posteriore, inprimis dextra maculae tendineae perspicuae. Valvulae arteriarum bene coierunt, in utroque ventriculo tenues et satis fenestratae fuerunt . . . . foramen ovale perfecte clausum . . . Caro musculosa ubivis coloris pallidi, subflavi. . . Aorta, ubi valvulae connivent, cum maculis diversis, aliquantum elatis, adipose degeneratis. Circuitus interior vasis hoc loco 5·6 centm., dum circuitus arteriae pulmonaris, ubi valvulæ connivent, 6·7 centm. Aorta toto in tractu angusta, tenuis et specie quasi magis infantili, ceterum valde elastica. . . Tunica intima aortae ascendentis et carotidum ferme normalis. In regione ligamenti arteriarum aorta ad circuitum interiorem 4·5 centm. per locum cymatii instar prominentem coangustata est. Ab hoc loco usque ad bifurcationem commutatis quaedam singularis observari poterat, modo magis ad parietem posteriorem, modo ad anteriorem pertinens. Cernebatur in elevationibus quibusdam undulatis et inter se conjunctis tunicae intimae, quae saepissime ovatae ad glandularum Peyeri ordinem in acervos constructae videbantur. In circuitu quoque ramorum, praesertim deorsum deflectentium concretiones parvae

Schünemann gives the history of a lad, aged 21, who bled to death after the removal of a molar tooth; the *post mortem* appearances recall those of the foregoing case; there was fatty degeneration of the fibres of a heart, somewhat enlarged; the liver also enlarged and fatty; together with a general want of blood throughout the body. But besides this there was an unnatural condition of the vessels: their walls were in some places unusually thin, flaccid, and transparent.[1]

Changes in the heart have been rather more frequently observed. A writer in 1818, commenting on the examination of a bleeder recorded by the two brothers Buel, says that "we have witnessed the examination of the body of a young man who died from nasal hæmorrhage, and who was represented to have been subject to bleeding to a great extent from the slightest causes,

atque in ostiis arteriarum lumbalium infimarum maculae magnae scleroticae exstabant.

"Elevationes, quas commemoravimus, undulatae jam ad tunicam mediam pertinent, quae ex his albide obnubilatur; tunica intima autem, fibris longitudinalibus contexta, accurate perspecta strias maculasque subflave albas ostendebat per degenerationen adiposam exortas. Maculae hujus generis singulæ partem convexam arcus aortae obsidebant.

"Cum in corde, tum in vasis majoribus copia mediocris sanguinis bene concreta inventa est. . .

"Exploratio microscopica cor degeneratione adiposa modice correptum, arteriarum tunicam intimam multis locis valde correptam ostendit; nihil tamen patefecit, quod ad arteriarum minorum et capillarium mutationes pertineret. In illis elementa adeo muscularia facillime et largiter sejungi poterant atque in arteriis tantummodo minoribus femoris passim inter fibras elasticas guttae dispersae adipis exstabant. Neque in nervis quidquam a norma discrepans detectum."

[1] Schünemann, *Arch. f. path. Anat.* Bd. xli. p. 289.

CHAP. VI. in which the heart was found to be of four or five times the usual size, but without any marks of disease. The extraordinary bulk of that organ arose from a preternatural development of its muscular structure."[1] Schneider found in the body of a lad, aged 17, who belonged to a bleeder family, and who died of bleeding from the nose, both pleuræ and the pericardium unnaturally filled with a quantity of serous fluid, the heart enormously enlarged,[2] containing no blood, the wall of the right ventricle remarkably delicate, and thin like membrane, the wall of the left ventricle unnaturally tough and thick; the valves and chordæ tendineæ like cartilage, and in some places almost as hard as bone; the coronary veins full of blood.[3] In the case already mentioned of a young student who bled to death after a mere scratch received in a duel, Escherich found all the organs natural; the heart very pale, and, saving a small coagulum in the right auricle, containing no blood; the foramen ovale partly open, and the septum of the auricles very thin and transparent with an opening nearly round and about 6‴ in diameter. Upon the side of the right ventricle there was a tendinous cord, scarcely 1‴ thick or .5″ long stretching to the opposite edge, and passing from back to front over the opening.[4] This must have assisted to close the opening in the septum of the auricles, and to diminish the evil effects,

[1] *London Medical and Physical Journal*, 1818, vol. xl. p. 431. This is the case referred to by Nasse. (Horn's *Archiv*, 1820, Mai-Juni, p. 428.).

[2] "ungeheuer gross"

[3] P. J. Schneider, (of Offenburg) Schmidt's *Jahrbb.* Bd. xxiv. p. 356.

[4] Escherich, quoted by Schneider, *loc. cit.*

if any, of such a communication. A similar thinness of the septum of the auricles was found by Schliemann in a Jew bleeder aged 15; a part of the septum of the ventricles of this boy was also deficient in muscular fibres and only closed by a thin transparent membrane; the pulmonary artery was unusually narrow and as thin as a vein.[1] Gavoy also found in a boy, aged 14, the subject of hæmophilia, and who died in the hospital at Strassburg, hypertrophy of the heart and thinness of the walls of the pulmonary artery.[2] Besserer noticed in a boy aged 6, who is said to have died of 'arachnitis,' that the left heart was hypertrophied, and contained much white and firm fibrinous coagula.[3] In one of Grandidier's cases, the only morbid appearance was a thinness of the right heart.[4] Schönlein seems to have thought the round and fœtus-like appearance of the heart to be constant in this disease, and to denote its connexion with cyanosis.[5] Especial weight was laid upon the imperfect development of the heart, the patency of the foramen ovale, and the deficiency of the muscular fibres in the walls.

Mutzenbecher examined the body of a boy who died from the bleeding into the connective tissue after a fall upon the chest. The whole of the intermuscular and subcutaneous tissue was full of dark coagulated blood.

[1] Schliemann, quoted by Grandidier, *op. cit.* p. 85.

[2] Gavoy, Canstatt's *Jahresbericht für* 1862, Bd. iv. p. 155. Abstract of *L'Hémophilie*, Thèse de Strasbourg, 1861.

[3] Besserer, Canstatt's *Jahresbericht f.* 1845, Bd. ii. p. 29.

[4] Grandidier, *op. cit.* p. 31.

[5] Schönlein, *Vorlesungen ueber Path. u. Ther.* 3tte Auflage, 1837, Bd. ii. p. 63.

CHAP. VI. There were also some extravasations of blood in the lungs.[1]

There are two cases shortly mentioned by Mr. Lane,[2] as occurring in the practice of Dr. Wilson, where death was caused by extravasation of blood within the cranium, as a consequence of blows on the head. Very similar to these two cases is the account given by Dr. Cousins of a lad of 16 who fell forwards in an epileptic fit, struck the forehead on the floor, and died. At a *post mortem* examination made 48 hours after death, an ecchymosis was noticed on the forehead and "a moderate amount of effused blood was found under the pericranium, corresponding in situation to the external injury. On removing the skull and dura mater, a thin layer of blood appeared covering the anterior two-thirds of the left hemisphere. The brain was congested throughout, and a considerable extravasation was also found at the base and upper part of the spinal cord. On section, a cavity was discovered in the anterior lobe of the left hemisphere about the size of a small walnut. Its walls were irregular, and of a light brownish colour. The cavity was empty, and it did not encroach anywhere upon the surrounding grey matter."[3] The lungs and heart are said to have been healthy.

[1] Mutzenbecher, quoted by Grandidier, *op. cit.* p. 85.

[2] Lane, *Lancet*, 1840, Oct. p. 187. These cases belonged to the same family as those described by Mr. Wilson in his *Lectures on the Blood*, &c.

[3] Cousins, *Medical Times and Gazette*, 1869, vol. ii. p. 278. The epileptic attacks dated from a fall on the left forehead 7 months before death: memory and mental power were much impaired.

In a case recorded by Liedbeck of Stockholm, a lad of 16, the subject of hæmophilia, received a blow upon the right temple; the temporal muscle became infiltrated with blood, and death followed. The examination after death showed that there was an extravasation of blood between the membranes at the base of the brain: this blood was coagulated, but that in the heart was not. All the other organs were found natural; but the vessels were not examined: this was also the case in this patient's brother, who died, at the age of 19, of hæmorrhage following the extraction of a tooth.[1]

Dr. Buss has recorded a case in which hæmophilia was associated with a misplaced spleen. The patient, a young man, aged 21, was seized with symptoms of peritonitis six days before death. On opening the abdomen, 24 hours after death, the intestines were found surrounded by a large quantity of grumous blood. Beyond great pallor, nothing amiss was noticed with the liver, kidneys, pancreas, and intestinal tract. On searching for the spleen, it was found resting on the internal iliacus muscle in the left iliac fossa; it was double the natural size, soft, and ruptured at its internal border. The thoracic viscera were somewhat pale and flabby.[2]

That much light should be thrown upon the pathology of a disease like hæmophilia by coarse anatomical examination was not, perhaps, to be expected. The malformation of the heart, which seems more frequently

[1] Björkman and Liedbeck, quoted by Huss, *Archives gén. de Méd.*, 1857, vol. ii. p. 178.

[2] Buss, *Medical Times and Gazette*, 1868, vol. ii. p. 530.

CHAP. VI. than any other tangible lesion to accompany hæmophilia, may perhaps be looked upon as another expression of the imperfect development of the whole vascular system. The observations on the greatly diminished thickness of the arteries are important; and it is to be regretted that three of these cases were examined before the microscope was brought into such general use as at present, and thus valuable opportunities of widening our knowledge were lost. In Lemp's case, however, Virchow could find no alteration of the small arteries or capillaries: nor could Morel in Gavoy's.[1] Should any opportunity hereafter occur to examine the capillaries after death, it would be best to take those parts which were most subject to bleedings during life; for example, the mucous membrane of the nose, when the patient had died of epistaxis. The microscopical observation is, it must be confessed, full of difficulty, and requires very many concurrent favourable circumstances; but no opportunity for making it should be lost.

It is unfortunate that the lower animals should be quite free from hæmophilia:[2] they would otherwise have afforded very valuable materials for the most in-

[1] As quoted by de Fleury, *Mém. de la Soc. méd.-chir. de Bordeaux*, 1866, t. i. p. 305.

[2] The case described by Schutt (Schmidt's *Jahrbücher*, Bd. cxxiii. p. 117) of a hæmorrhage from the skin and other parts, in a horse, seems to belong rather to purpura, or some allied affection, than to hæmophilia: and the case which Mélon (Virchow's *Jahresbericht f.* 1868, Bd. i. p. 520.) has described under the name of hæmophilia in the horse does not, from the description, appear even to belong to the class of hæmorrhagic diathesis.

structive observations upon the ætiology and pathology of the disease. CHAP. VI.

The pathology of hæmophilia is still buried in the deepest obscurity: nor are any glimmerings of light to be discovered in the numerous theories which have been advanced as to the nature of the disease. Some writers regard hæmophilia as an anomalous form of other diseases; or as dependent upon some alteration in the blood, or in the blood and blood vessels together, or as a disease of the whole vascular system; or a disease of the capillaries only. These various theories will now be considered more at length.

Consbruch,[1] Elsässer,[2] and Krimer[3] all mention the 'gout' in their reports, either the patients themselves or their relatives being subject thereto. Nasse mentions this with approval: he says that gout is both hereditary, and far more frequently seen in men than women; that the vascular system in gout often suffers, as the tendency to bleedings and hæmorrhoids testify.[4] Rieken regarded hæmophilia as an anomalous variety of gout and grounded this assertion upon the four following propositions:

"1. The tendency to extreme hæmorrhages has been of late observed only in those persons whose parents or grandparents have suffered from gout.

"2. In those members of bleeder families who have escaped the tendency to hæmorrhage, gouty paroxysms may often be observed.

[1] Consbruch, Hufeland's *Journal*, Bd. xxx. Stück v. p. 117.

[2] Elsässer, *ibid.* Bd. lviii. Stück ii. p. 97.

[3] Krimer, Horn's *Archiv*, 1820, Mai-Juni, p. 413.

[4] Nasse, *ibid.* p. 429.

CHAP. VI. "3. In bleeders themselves, gouty paroxysms are nearly always seen, and sometimes an alternation of the joint affection with the bleeding.

"4. Gout is a disease which stands in a very close relation to the blood and blood vessels, and often appears to be a direct cause of hæmorrhage."[1]

Unfortunately, none of these propositions can now be maintained. As to the first and second, hæmophilia is by no means so exclusively seen in gouty families: gout does occur in a certain number of bleeder families, but hæmophilia commonly occurs without any mention of gout being detected in the family history. Then as to the third proposition, the swelling of the joints peculiar to hæmophilia has been mistaken for true gout, a mistake not uncommon among the earlier writers on hæmophilia. The fourth proposition may, however, find defenders at the present day. I am aware that a very general impression exists that gout favours the occurrence of hæmorrhoids and bleedings. But out of 50 of my patients at Saint Bartholomew's Hospital, who suffer from well-marked gout, of duration rarely less than 10 years, I have found on careful inquiry that not more than 3 have at any time in their life been subject to hæmorrhoids, and none subject to bleedings from other parts. These observations have led me to suspect very greatly the statement that bleedings are common in gout, and this is a point which ought clearly to be made out, before a theory of hæmophilia be built upon it.

[1] Rieken, *Neue Untersuchungen in Betreff der erblichen Neigung zu tödtlichen Blutungen*, Frankfurt a.M. 1829, p. 87, *et seqq.*

Schliemann looked upon hæmophilia as a disease intermediate between cyanosis and scrofula;[1] and Heyfelder, as intermediate between gout and scrofula.[2] The meaning of the word scrofula is so undetermined that it is not worth the time to stay to discuss such opinions. CHAP. VI.

S. G. Vogel thought that a scorbutic state of the blood might occasionally lie at the bottom of the phænomena; but this opinion seems intended by him to be applied to only one case, that of Rave's; which Grandidier regards as intermediate between scurvy and true hæmophilia.[3]

A relation to cyanosis was thought of early in the history of hæmophilia. Nasse in 1811 drew a distinction between the blood in cyanosis and the blood in hæmophilia;[4] and J. F. Meckel, commenting on the American cases, says that cyanosis is plainly only a higher grade of hæmophilia.[5] Later on, Nasse compared the two diseases; both present bleedings difficult to check; both affect the male sex; both show a great mortality early in life; in both there happens occasionally a general blueness of the body; and in both, also, the patients are exceedingly passionate.[6] But Schönlein was the most active supporter of the theory of the connection of cyanosis with hæmophilia; he appears to

[1] Schliemann, *De dispositione ad haemorrhagias perniciosas haereditaria*, Diss. Inaug. Wirceb. 1831, p. 45.

[2] Heyfelder, *Medizin. Zeitung (Vereins)*, 1833, p. 216.

[3] S. G. Vogel, *Handb. d. pract. Arzneywissenschaft*, Stendal, 1820, Neue Ausgabe, Theil v. p. 14.

[4] Nasse, Reil's *Archiv f. d. Phys.* 1811, Bd. x. p. 266, Note.

[5] J. F. Meckel, *Deutsches Archiv f. d. Phys.* 1816, Bd. ii. p. 140.

[6] Nasse, Horn's *Archiv*, 1820, Mai-Juni, p. 429.

CHAP. VI. have made many *post mortem* examinations in which a round and fœtal shape of the heart was observed; as as well as a deficiency in the muscular walls, a membranous septum only being present, and the foramen ovale patent.[1] In his nosology, the disease is placed between cyanosis and chlorosis. Schönlein doubtless laid too much stress upon the malformation of the heart, yet he did good service by drawing attention to the ill-developed condition of this organ in some cases, a point which will be hereafter more dwelt upon.

The theory of some alteration in the blood is a favourite explanation of the phænomena of hæmophilia. In 1811, Nasse sought to explain the unnatural fluidity of the blood, to which he attributed the disease, by a hyperoxydation;[2] but in 1820, he attributed this unnatural fluidity to a fault of development, the blood remaining in a lower stage of growth.[3] The same opinion had been expressed by Meckel with the addition of a comparison of the blood in hæmophilia to that of the Cetacea.[4] The belief in the extreme fluidity of the blood depended upon the older observations, now known to be incorrect, of the absence of coagulation: and this circumstance, joined to an assumption of an alteration in the blood vessels as well, was the most common theory of the disease for many years, Rokitansky having lent the weight of his authority to the statement that in hæmophilia there was a thin watery condition of the

[1] Schönlein, *loc. cit.*

[2] Nasse, *op. cit.* p. 267, Note.

[3] Nasse, *op. cit.* p. 431. Grandidier says that Nasse withdrew this opinion in 1843.

[4] J. F. Meckel, *op. cit.* p. 138.

blood, joined to a great delicacy of the vessels, and liability of these to injury.[1] The theory of an increased fluidity of the blood has of late been revived by Gavoy. He believes that there is something in the blood which renders it more fluid, an alkaline salt for instance.[2] His analyses, however, do not show a larger percentage of salts than is usual in health.[3]

The theory of an alteration of the blood, especially if this alteration be attributed to an increase in the amount of alkaline salts, has gained some support from the observations of Prussak. He injected a 2 per cent. solution of chloride of sodium into the lymph sacks of frogs, and found that the red corpuscles everywhere began to escape through the uninjured walls of the vessels, and to be visible in the tissues around. Chloride of sodium was also daily injected into the connective tissue of a rabbit, and after death, numerous ecchymoses were found in all the organs.[4]

The hypothesis of a change in the blood may be

[1] Rokitansky, *Handb. d. allg. path. Anat.*, Wien, 1846, Bd. i. p. 167. It is only just to mention that this passage does not appear in the third edition of this work.

[2] Gavoy, quoted by de Fleury, *Mém. de la Soc. méd.-chir de Bordeaux*, 1866, t. i. p. 307.

[3] For the analyses, see p. 61.

[4] Prussak, *Sitzungsb. der mathem.-naturwissen. Classe der kaiserl. Akad. der Wissensch.*, Wien, 1867, Bd. lvi. Abth. ii. p. 13. I have several times repeated these experiments on the frog with success; but I have not been able to produce these minute hæmorrhages by the injection of any other halogenous salt, paying especial attention to the action of the iodide and bromide of potassium, after the use of which Ricord and Walshe are said to have noticed a disposition to hæmorrhage.

CHAP. VI. serviceable in the explanation of a temporary hæmorrhagic diathesis; but I doubt very much if such an alteration be the source of a congenital disease, lasting, like hæmophilia, throughout life. Besides, there is not one recent observation of any deviation in the blood from the standard of health. I do not say that such will not be found: but there is at present no evidence of such alteration.

In any future analyses of the blood in hæmophilia, it will be necessary to make exact observations on the amount of salts present. Especial attention should be paid to the amount of chloride of sodium. Unfortunately, the method of estimation which is used by the chemists for any one salt is still very defective, being in fact little more than a guess; so that until the process for estimating a salt separately shall have been perfected, Chemistry cannot be relied upon with much confidence to give assistance in this direction. It would always be well, however, to ascertain the gross amount of salts contained in the blood; and, if possible, the amount contained in the plasma and corpuscles respectively.

The theories which refer the phænomena of this disease to some alteration in the vessels will next be considered. Autenrieth and Wedemeyer think that there is a paralytic condition of the capillaries, brought about by their imperfect development.[1] Meinel also is of

[1] Autenrieth and Wedemeyer, quoted by Wachsmuth, *op. cit.* p. 42. Wedemeyer (*Untersuchungen ueber den Kreislauf des Bluts*, Hannover, 1828, p. 327) does not mention hæmophilia; only scurvy and the *Morbus maculosus Werlhofii* are spoken of as explicable by a theory allied to that given in the text.

opinion that there is a congenital imperfect vitality of the capillaries from which they are unable to resist the flux of blood to any part, and thus an escape of blood takes place with or without a rupture of the walls.[1] Wachsmuth assumes a congenital disproportion between the increased vitality of the blood and the power of resistance possessed by the capillaries which are too delicately organized, and sometimes wanting in tone.[2] CHAP. VI.

All depends, in this theory, upon the meaning of the word vitality: Wachsmuth seems to think that it is allied to something which was called hyperoxydation by Nasse. I must, however, confess my inability to understand what is meant. But Resal has adopted it, giving this definition to the word vitality: an increased power of making blood. This increased power of making blood, whether congenital, hereditary, or acquired, causes a reaction in the organism, and thus hæmorrhages occur at those parts of the capillaries which are weakest or suffer from atony.[3] Resal's hypothesis rests upon the assumption that there exists in hæmophilia a power of quickly renewing the blood, when much has been lost by bleeding. Some few observers have noticed this in their patients, but it is far from being a universal law in hæmophilia. After a great hæmorrhage, these persons suffer from anæmia for many months; the power of rapid convalescence is not a feature of the disease.

There is yet another theory of a disturbed innerva-

[1] Meinel, quoted by Grandidier, *op. cit.* p. 114.

[2] Wachsmuth, *op. cit.* p. 43.

[3] Resal, *op. cit.* p. 75.

CHAP. VI. tion of the capillaries. Cochrane attributes the hæmorrhages to the absence of nervous influence in the seat of the disease and consequent decreased vital action. "Owing to this decrease of nervous power, the unresisting vessels in the congested part become enlarged; and those of them which admitted only the transparent and more fluid portion of the blood, now admit the red globules, distending their calibre, and destroying their tonicity: hence hæmorrhages, &c."[1]

Tamme Beth was inclined to believe in the nervous character of the disease, and spoke of the striking value of animal magnetism.[2] Martin attributed the symptoms to some nervous influence: all the bleeders known to him were unable to indulge in mental or bodily exercise without fear of bleeding; and mental emotions, terror, fear, such as might be caused by scoldings and small punishments, of a certainty produced hæmorrhages.[3] Reinert agrees with this, and believes further in some alteration of the vaso-motor nervous system, an enfeebling of the sympathetic which allows the vessels to dilate even to bursting.[4]

Otte was led to entertain the hypothesis of an alteration in the nervous system by observing the temporary disappearance of the hæmorrhagic diathesis in some bleeders. He noticed especially in his own patient, who suffered from epileptic attacks, that although the boy was accustomed during the convulsions to strike himself violently against surrounding objects, yet no ecchy-

[1] Cochrane, *Lancet*, 1842, April, p. 149.

[2] Tamme Beth, quoted by Grandidier, *op. cit.* p. 114.

[3] Martin, quoted by Reinert, *Ueber Haemophilie*, Diss. Inaug. Göttingen, 1869, p. 23.

[4] Reinert, *loc. cit.*

moses were produced. Was this due to some nervous influence upon the vessels during the paroxysm? The nervous alteration causing the hæmorrhages may resemble that exercised on the vessels of the neck and ear of the rabbit when the sympathetic in the neck is divided. So in hæmophilia, one or two nerve tracts only may be affected at one time, and the various phænomena may be caused by occasional alteration in the degrees of tension in the vessels, while the place, where this alteration of tension occurs, varies. The difficulty of arresting the hæmorrhage may be explained on the same theory: the blood continues to flow until the nervous influence causing the congestion and stasis has ceased to act, thus allowing the walls of the vessels again to recover their normal tone, so that an opportunity is given for the formation of a thrombus; or, in the case in which the blood is poured out into the tissues, the blood may coagulate around the vessels, and by its pressure, cause a cessation of the hæmorrhage, before this point of normal tone is reached. He closes his argument by some remarks on the cases in which a hæmorrhagic diathesis has been set up after great mental emotion.[1]

The theories of Martin, Reinert, and Otte are identical in principle, and may be discussed together; they all make the essence of hæmophilia to lie in some alteration of the functions of the vaso-motor nervous system. Martin seems to base his theory on the assumption that mental emotion produces bleeding in hæmophilia with great ease. Now as a matter of fact,

[1] Otte, *Ueber die Bluterkrankheit,* Leipzig, 1865, p. 41, *et seq.*

CHAP. VI. mental emotion is not mentioned by the great majority of observers as an exciting cause of hæmorrhage; there are only three writers who speak of it; and therefore any theory based upon this must fall, unless a far greater number of cases be brought together. As to the influence of the vaso-motor nervous system: it may be well discussed, whether the present state of knowledge warrants the belief in the power of the nervous system to produce hæmorrhage. When the sympathetic is divided in the neck of rabbits great hyperæmia ensues, but no hæmorrhage, although Bouchard has succeeded in producing ecchymoses in the paralysed ear by raising the blood pressure.[1] The experiments of Pincus,[2] and of Moritz Schiff[3] show only that deep alterations of nutrition, hyperæmia and sloughing, not simple hæmorrhages, follow the injury of vaso-motor nerves or of the medulla oblongata. Indeed the latter observer found that no hæmorrhages followed the removal of the nerves of the stomach.[4] The observations of Brown-Séquard upon the hæmorrhages in remote or-

[1] Ch. Bouchard, *De la Pathogénie des Hémorrhagies*, Paris, 1869, p. 80. The superior cervical ganglion was removed from the left side of a rabbit, and the aorta tied below the renals. Small hæmorrhagic points were soon after observed in the paralysed ear. But in two other experiments (p. 121) he failed, even after ligature of both jugulars, to produce ecchymoses.

[2] Pincus, quoted by Samuel, *Die trophischen Nerven*, Leipzig, 1860, p. 45.

[3] M. Schiff, *Lezioni di fisiologia sperimentale*, Firenze, 1866, Lez. xxix. p. 289 *et seq.*; Lez. xxxix. p. 393 *et seq.*

[4] M. Schiff, *Leçons sur la Physiologie de la Digestion*, Florence, 1867, Lecture xxxv.

gans which follow injury of the nervous centres are important :[1] but it is quite possible that the explanation of these hæmorrhages may fall outside the nervous system. Thus at the present moment there seems scarcely enough evidence to allow us to assume the fact that hæmorrhages may be caused by the action of the vaso-motor system only, although, at the same time, such an assumption is highly probable; and the vaso-motor nerves may hereafter be found to have a great share in the pathology of hæmophilia. The theory of innervation is almost the only one which offers any explanation of the phænomenon of the disappearance and aggravation of the hæmorrhagic diathesis at varying times.

It is necessary just to mention the view which Grandidier has propounded with reference to hæmophilia. It is a union of two preceding theories: both the blood and capillaries are at fault; the blood is wanting in fibrin, and there is an imperfect action in the atonic capillaries, the walls of which are thin and readily torn. He seems also to think that there is a want of contractile power in these latter, which helps to keep up a hæmorrhage once established.[2]

Nearly 20 years ago, Virchow drew attention to the important part which the spleen plays in all hæmorrhagic diatheses.[3] Of the truth of the connexion between the organ and the constitutional state, no one can doubt, after so exquisite an example as that which occurs in leucæmia: but I am scarcely inclined to think that these remarks of Professor Virchow were

[1] Brown-Séquard, *Lancet*, 1871, vol. i. p. 6.

[2] Grandidier, *op. cit.* p. 115.

[3] Virchow, *Handb. der spec. Path. u. Ther.*, Erlangen, 1854, Bd. i. p. 247.

CHAP. VI. intended by him to apply to hæmophilia; they seem rather intended to refer to the temporary hæmorrhagic diatheses which occur in the course of so many diseases, than to be any attempt at the explanation of a congenital permanent disease like hæmophilia.

Of greater interest is his commentary upon Lemp's case, already mentioned.[1] The whole of the appearances in this case recall those seen in chlorosis. In chlorosis, the development of the heart and aorta is very backward; later, however, follow enlargements of the heart. Bleedings are common and violent in chlorosis, and they might have some relation to the alterations in the arterial walls: the round ulcer of the stomach always corresponds to the track supplied by certain arteries. There is much in favour of the congenital or early development of the predisposition to chlorosis. Have the narrowness and great elasticity of the arteries anything to do with hæmophilia? They may increase the blood pressure in the arteries, thus producing the disposition to bleed, and maintaining it when once established. The causes of a hæmorrhagic diathesis must be sought in an arrest of the growth of the vessels,[2] and it should be noticed that, in Lemp's case, the thymus was persistent.[3]

[1] See p. 80.

[2] "Hemmung der Gefässbildung."

[3] Virchow, Canstatt's *Jahresbericht f.* 1859, Bd. iv. p. 267. De Fleury (*op. cit.* p. 309) has also made the comparison between chlorosis and hæmophilia; but on quite different grounds from those of Professor Virchow, and also, it would appear, in ignorance of his views. The comparison seems based chiefly on the anæmia which sometimes exists in hæmophilia, and also on the pica which has been noticed in some few cases.

It is impossible not to remark, in speaking of this comparison between hæmophilia and chlorosis, with all the deference that is due to any opinion of Professor Virchow, that bleedings are certainly not so common in the latter disease as might be supposed from the foregoing description. In fact, hæmorrhage is, in my necessarily short experience of chlorosis, one of the symptoms which are the exception, and not the rule;[1] and this circumstance appears to me to be the weakest part of the theory which has just been set forth. Of the constant presence of a narrow aorta in chlorosis, it is unnecessary here, nor perhaps does it become me, to speak.

On reviewing the present state of our knowledge of the pathogeny of hæmorrhages, it would seem probable that, in nearly all cases, an alteration of the vessels precedes the effusion of blood:[2] hæmorrhages in chronic diseases, without previous disease of the blood vessels, are exceedingly rare. It is highly probable, then, that in hæmophilia, a chronic disease, some change in the vessels is present. As yet, it is true, none has been discovered; but the following hypothesis has seemed to me capable of explaining some of the phænomena of hæmophilia.

[1] I am aware that Trousseau has pointed out the fact that menorrhagia and epistaxis are sometimes the consequences, and not the causes, of chlorosis. But he does not regard these phænomena as very common. Is it possible that chlorosis may convey in Germany a notion different from that in England?

[2] Even in some acute hæmorrhagic diseases, as purpura, disease of the blood vessels has been detected. (Wilson Fox, *British and Foreign Med.-chir. Review*, 1865, Oct. p. 490.)

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In hæmophilia there is an imperfect development of the whole vascular system. In many cases, the heart retains an appearance similar to that in the fœtus, and in parts, the muscular fibres are wanting in the ventricular or auricular wall, being replaced by a membranous septum only. In others, the arteries are exceedingly thin, transparent, and unable to preserve a circular section. These appearances render it probable that there is an arrest of development, or backwardness of growth, in the heart and blood-vessels. Now true hæmophilia is a congenital disease, and it may be that the fœtal state of the vascular system persists in extra-uterine life. Newly-formed vessels are very liable to hæmorrhages, spontaneous and traumatic: the new-born infant bleeds much more readily, and for a longer time, than the adult. The vessels of newly-formed granulations, of rapidly growing tumours, bleed upon very slight provocation. If the vessels in hæmophilia were permanently in the fœtal or newly developed state, frequent and long-continued bleedings might well be expected from them. And in this case it would not be surprising that not much alteration should be detected with the microscope; which has happened in the two cases[1] in which such examination was made.

The occasional disappearance of the hæmorrhagic diathesis in cases where the patients have reached a certain age, may be explained on this hypothesis. In most of the cases in which it has been recorded, the patients have lost the disposition to hæmorrhage between the 25th and 30th years of life, a time about which the

[1] Gavoy, *loc. cit.* Lemp, *loc. cit.*

human frame is said to become fully developed, and in which development it is possible that the vascular system may share.[1]

It will be at once observed that this theory can offer no explanation of the occasional temporary disappearance of the diathesis. It is, also, only the removal of the difficulty one step backwards. The progress of pathology will soon show whether it is, or is not, worthy of any further consideration.

I am not acquainted with the record of any examination, after death, of the joints of a patient suffering from the swelling common in hæmophilia.[2] The nature of the swelling is as obscure as the rest of the pathology of this disease. Dubois long ago asserted that the fluid, so plainly contained within the capsule of the joint, was blood.[3] This statement was, however, everywhere received with great reserve, no proof having been brought

[1] Since these lines were written, I find that I have no less an authority than that of Professor Virchow in support of this theory. Speaking of the delicacy of newly formed vessels and their liability to bleed, he says: "So möchten sich manche erbliche Formen hämorrhagischer Diathese erklären." (*Handb. d. spec. Path. u. Ther.* Bd. i. p. 240). At present, Professor Virchow does not seem to have any theory to offer to explain the pathology of hæmophilia. See the fourth edition of *Die Cellularpathologie*, Berlin, 1871, p. 257.

[2] Lemp, indeed, (*De haemophilia nonnulla*, p. 18) records the examination of the knee long after all inflammation had subsided: In articulatione genu tota fere membrana synovialis multo pigmento rubiginoso impleta et obtecta erat. Synovia vero valde imminuta, nec minus cartilagines paullum dissolutae erant.

[3] Dubois, *Gaz. méd. de Paris*, 1838, p. 43.

CHAP. VI. forward by Dubois, until recent observations showed the possibility of an extravasation of blood within the joint being the cause of the swelling. In Reinert's case, the capsule of the shoulder-joint suppurated, whereupon a great quantity of blood escaped,[1] and, it is assumed by the author, escaped from the interior of the joint. Assmann, also, saw a considerable quantity of fluid blood escape upon puncture of the swollen knee of a bleeder.[2] It is very unsafe, however, with Reinert, to infer that an effusion of blood into the joint precedes all the articular swellings: it is doubtless an explanation of many cases; but scarcely, I am inclined to believe, of all. In the absence of all knowledge of the morbid anatomy of this state of the joints, it is best to remain silent until something certain be attained.

[1] Reinert, *Ueber Hämophilie*, Diss. Inaug. Göttingen, 1869, p. 12.

[2] Assmann, *Die Hämophilie*, Diss. Inaug. Berlin, 1869, p. 12.

CHAPTER VII.

DIAGNOSIS AND PROGNOSIS OF HÆMOPHILIA.

The diagnosis of hæmophilia presents, in its pronounced form, but little difficulty. It is otherwise, however, when an incomplete and low grade of the disease is seen, especially if the patient should then happen to be a woman. It is easy to make the diagnosis when a boy has suffered, since early infancy, from all kinds of bleeding, especially traumatic, and the joints have as well been repeatedly swollen.

But in the second degree of the disease, when spontaneous bleedings only have been noticed, and no liability to traumatic hæmorrhages exists, a great deal of caution has to be exercised; for it is no uncommon thing for boys to suffer repeatedly, before puberty, from severe epistaxis.[1] Several points must be enquired into: the existence of hæmophilia among the kinsmen will greatly

[1] "Narium haemorrhagia, uti "regulariter et sincerius competit "junioribus, pueris, et adoles- "centibus, in sexu maxime virili; "Ita citra plane peculiares ra- "tiones, haereditariae disposi- "tionis, aut adsuetudinis, aut "externarum commotionum in- "solentiorum, non evenit etiam, "nisi manifestius plethoricis." Stahl, *Theoria Medica Vera*, Halae, 1708, p. 701. Stahl several times speaks of an hereditary disposition to hæmorrhage, which might, by an earnest searcher after allusions to hæmophilia, be construed into descriptions of that disease. But I do not think that he was really acquainted with it.

CHAP. VII. strengthen the diagnosis;[1] the absence, on the other hand, of any great hæmorrhage when severe wounds have been inflicted is against the diagnosis, and especially if no abundant hæmorrhage have followed the taking out of a tooth; for this operation may be looked upon as a touchstone for a bleeder. Again, if the hæmorrhages have taken place from one part only, and have not been of a very long duration, the case is less likely to be hæmophilia: but if the blood have come from more parts than one, and the patient have suffered from early life, while the bleedings have always lasted a long time, the case may be allowed to be placed in the lower grade of hæmophilia.

The foregoing remarks apply chiefly to boys. In women, hæmophilia is never seen in its most intense form: in them it appears in the second or third degree, not often showing any tendency to traumatic hæmorrhages. When ecchymoses are the only hæmorrhagic appearance, the diagnosis of hæmophilia should not be allowed, unless the patients belong to a bleeder family: for who has not seen women in which the lightest touch does not produce extravasations of blood?

There are also certain hæmorrhagic diatheses in women, which require to be distinguished from the second degree of hæmophilia. The diagnosis is often a matter of difficulty: it will be treated of more fully in Chap. X., which is devoted to the consideration of this disposition. It will be sufficient here to remark

1 The presence of real hæmophilia must be ascertained to be any help to the diagnosis; for an hereditary disposition to bleed, especially from some particular organ, is by no means uncommon.

that the diagnosis turns chiefly on the absence of the diathesis before puberty, and of any predisposition to hæmophilia, either in the patient's kindred or children. CHAP. VII.

When a hæmorrhagic diathesis appears in very young children, the question of hæmophilia may sometimes be raised. Cases of umbilical hæmorrhage, especially when accompanied by jaundice, often prove fatal after having shown signs of an intense hæmorrhagic disposition, the blood issuing from all parts of the body. Cases of this kind plainly do not belong to hæmophilia: they occur in children of both sexes: very rarely is any hereditary disposition present: as the great majority of the children die, there is no means of proving that in after life they are subject to hæmorrhages; but in those, however, who survive, no tendency to hæmorrhage has been remarked.[1]

The same remarks apply to a similar disposition in somewhat older children, who, within a few days or weeks of birth, acquire an intense hæmorrhagic diathesis, and at last die of the bleeding. To this class belong the often quoted case of du Gard,[2] and the cases of André,[3] Burdach,[4] Koch,[5] &c. It may be remarked that hæmophilia rarely causes the death of the patient before the end of the first or second year; when death occurs earlier, the case should be viewed with suspicion, unless the patient inherit the disposition.

[1] Grandidier, *Die freiwilligen Nabelblutungen der Neugeborenen*, Cassel, 1871, p. 85.

[2] See above, p. 20.

[3] André, Schmidt's *Jahrbücher*, Bd. lxxii. p. 142.

[4] Burdach, *Medic. Zeitung* (*Vereins*), 1836, p. 169.

[5] Koch, Schmidt's *Jahrbb.* Bd. cxxxix. p. 173.

CHAP. VII. Of the diagnosis between purpura, scurvy, and other hæmorrhagic diseases on the one hand, and hæmophilia on the other, it is scarcely necessary to speak. Hæmophilia is always congenital and persistent, while these diseases arise during the lifetime of the patient, and are usually of short duration.

The swelling of the joints, so common in hæmophilia, may readily be mistaken for some forms of rheumatism, nor are there any trustworthy means for its distinction from any other affection accompanied with a large excess of fluid in the joint. The diagnosis depends upon the circumstance of the swelling occurring in a person already known to be the subject of hæmophilia. Formerly the diagnosis was practically of more importance than at present; for therapeutical measures, highly dangerous in the subjects of hæmophilia, such as the application of leeches, &c., were commonly resorted to for the relief of inflammation. With white swelling, the swelling of hæmophilia could scarcely be confounded save in the earliest stages: the progress of the two diseases is altogether different.

The prognosis of hæmophilia may be considered under two heads: during the bleeding; and during the absence of bleeding.

During the bleeding, the prognosis depends upon the length of time that the bleeding has lasted, and upon the amount of blood lost, together with the age and previous health of the patient. Schönlein says that the first bleeding is rarely fatal.[1] The bleeding seldom

[1] Schönlein, *Vorlesungen über Path. u. Ther.*, 1837, 3tte Auflage, Bd. ii. p. 63.

stops until nearly all the blood has left the patient's body: those cases in which there is one profuse hæmorrhage, which causes fainting, seem to be, on the whole, more favourable than long-continued constant oozing. The younger the patient also, the worse the prognosis; good general health, immediately preceding the bleeding, makes the prognosis more favourable. The kind of injury in a traumatic hæmorrhage influences the prognosis: the bleeding after the taking out of a tooth is especially dangerous; wounds caused by tearing and bruising are also thought to be more dangerous. Of spontaneous hæmorrhages, epistaxis is the most unfavourable to the patient; and, after that, bleedings from the bowel.

Before considering the remote prognosis of hæmophilia, it will be of advantage to take a review of the general course and termination of the disease.

Death by hæmorrhage is beyond doubt the most usual termination; and this very early in life, few living to be 21 years old. Out of 152 boys, subjects of this disease, Grandidier found that 133 died before attaining this age.[1] His numbers are:

During the first year there died[2]			20
Between	1— 7	„	61
„	7—14	„	36
„	14—21	„	16
„	21—28	„	7
„	28—35	„	5
„	35—45	„	3
Over	50	„	4
			152

[1] Grandidier, Schmidt's *Jahrbücher*, Bd. cxvii. p. 333.

[2] I believe that hæmophilia is rarely fatal during the first year:

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A glance at this table will show that the mortality amongst those who survive the age of 21 is somewhat less than at the ages below it: out of 71 who remained alive at 7, only 35 lived to be 14; while out of the 19 who lived to be 21, 13 survived to be 28; a difference of 50 per cent. to 70 per cent.

It is possible, however, that the tendency to hæmorrhage may be lost. In one of the earliest recorded cases, by Krimer,[1] it is said that the disposition to bleed began to disappear between the age of 25 and 28, and Saint-Vel speaks of a case where the disposition was lost at the age of 25.[2] I do not feel disposed to lay much stress upon the case of the younger Thore: a boy, without any hereditary disposition, was the subject of repeated hæmorrhages for the first six years of life: he then passed from observation; but being met with again at the age of 12, it was asserted that the hæmorrhagic tendency had disappeared ever since the last observation, a swelling of the knee having taken its place.[3] Bleeders are so frequently free from hæmorrhage for a length of time, even years, together, especially when the joints remain swollen, that a longer-continued observation is necessary before it can be confidently asserted that the disease has ever disappeared at this early age: it was probably a respite only, and not a

at all events symptoms rarely appear before the end of the first twelvemonth. The number in the text is caused by the admission of cases of umbilical hæmorrhage, &c.

[1] Krimer, reported by Nasse, Horn's *Archiv*, 1820, Mai-Juni, p. 418.

[2] Saint-Vel, *Union méd.*, 1865, t. xxvii. p. 516. It left behind an anchylosis of the hip joint.

[3] Thore, *Gaz. méd. de Paris*, 1856, p. 653.

release. Gintrac records a case where the hæmorrhages disappeared at 20 years of age; but in rather more than a twelvemonth, the patient became subject to epileptic seizures, and he died during one of these attacks towards the age of 24.[1] Lemp also mentions a case where a man, aged 26, had remained free from hæmorrhage for several years, and was enjoying excellent health at the time of observation.[2] CHAP. VII.

In one of Grandidier's families, the father lost the disposition at about 30 years of age; thereafter suffered from pains in the joints and 'asthma' until 64, and died when 70 years old.[3] In one of Mutzenbecher's patients the diathesis disappeared in the 37th year, but the right arm became contracted from the 'gout:'[4] in the 39th year, hæmorrhoids appeared, and the pains in the joints became much less severe. In one of Steinmetz' cases, the patient was 65 years old, and said that for the last 10 years he had been free from the hæmorrhagic tendency;[5] but that since that time he had suffered from pains in the limbs, pain in the head on

[1] Gintrac, *Cours théorique et clinique de Pathologie*, Paris, 1853, t. iii. p. 111.

[2] Lemp, *De haemophilia nonnulla*, Diss. Inaug. Berol. 1857. p. 17. "Ex compluribus tamen annis sanguinis profluvia cohibita sunt et vir nunc in aetatis anno vicesimo sexto sanitate optima fruitur."

[3] Grandidier, *op. cit.* p. 105. A case is also mentioned (p. 30) of a man in a bleeder family who lost the tendency to bleed; but the exact age is not given: he died in his 74th year of an apoplexy.

[4] Mutzenbecher, quoted by Grandidier, *loc. cit.* Probably some form of chronic rheumatism. True gout is rare in Germany; almost any joint affection is called gout by the public there.

[5] Steinmetz, Rust's *Magazin*, Bd. xxvii. Hft. ii. p. 379.

CHAP. VII. one side, and heartburn. In one of Consbruch's cases, it is stated the man was then quite free from the disease; but that he had the 'gout' worse, and that at the end of the paroxysm there appeared ecchymoses about the joint.[1] The age of this patient is not given. Hughes simply states, that, on the approach of old age, the tendency to hæmorrhage has been less manifest,[2] without giving any further details. Lebert's remark, that the disease has not been seen after the age of 40,[3] is disproved by numerous cases, even by one that he himself quotes.[4]

The remote prognosis of hæmophilia is indeed unfavourable. In all cases a life of restraint must be looked forward to; and most probably a life of suffering as well, broken only by rare intervals of something approaching to good health. The lot of these unfortunate persons must be very hard to be borne; but it is not the worst, for they have never known what it is to be well.[5] Even the prognosis as regards bare existence is, until puberty has been attained and passed some years, most unfavourable: out of 152 patients, only 19 lived to be 21.

There are certain circumstances which are thought

[1] Consbruch, Hufeland's *Journal*, Bd. xxx. Stück v. p. 117.

[2] Hughes, *American Journal of Medical Science*, 1833, vol. xi. p. 543.

[3] Lebert, *Arch. gén. de Méd.* 1837, sept. p. 56. "On n'a guère observé d'hémorrhagie constitutionnelle après l' âge de quarante ans."

[4] Lafargue's.

[5] Nessun maggior dolore,
Che ricordarsi del tempo felice
Nella miseria.
Inferno, Canto v.

But the same thought was expressed long before Dante by Boethius, *De consol. Philos.*, Lib. ii. Pros. iv.

to be favourable to the patient. A patient who enjoys good health between the bleedings will be more likely to pull through than a feeble debilitated boy. The social position has also an influence on the prognosis; those belonging to the upper and middle classes have a better chance than those of artizans. The sex is of considerable importance; as the prognosis is considerably more unfavourable to boys than to girls. The prognosis will also be more unfavourable if there be complications with other diseases, as rickets, disease of the heart or nervous system. All these circumstances, however, influence the prognosis but very slightly: the only point of much moment is the intensity of the disease; for if traumatic bleedings be absent, or only ecchymoses seen, the prognosis is much more favourable, one of the great sources of danger, the results of injury, being removed. Chap. VII.

After puberty, the prognosis is somewhat more favourable: the chance of the disposition to hæmorrhage being lost becomes a factor in it. This disappearance has, of all the recorded cases, happened only 9 times, omitting Hughes' cases and Thore's doubtful one: so that it cannot much be relied upon. Something also depends upon the trade of the patient; if it be one where small injuries are common, the case in so many of the occupations of the lower orders, the prognosis will necessarily be more grave.

It is not known if the prognosis be rendered more unfavourable by an hereditary transmission of hæmophilia.

CHAPTER VIII.

Treatment of Hæmophilia.

A description of the treatment of hæmophilia must necessarily be divided into several parts, corresponding to the different symptoms of the disease. The treatment proper to the traumatic and spontaneous hæmorrhages, and the prophylactic treatment between the hæmorrhages, will be considered separately; the manner, in which the swellings of the joints may be most successfully dealt with, will be described at the last.

Before considering the positive therapeutics of hæmophilia, it may be well to mention those procedures which are ordinarily used in other disorders, but which cannot be employed in hæmophilia without the risk of greatly injuring the patient.

First of all, any procedure by which blood is drawn, must be absolutely avoided; such as phlebotomy, the application of leeches, the lancing of gums for difficult teething, and scarifications of all kinds. Then, any measures by which a loss of substance, however small, is incurred, such as the use of blisters, or of the red-hot iron, should be employed with caution. There is one case recorded of the application of blistering plaister having been followed by fatal hæmorrhage; and it would always be well before employing blisters to ascertain what results attended their use on a former occasion. The hot iron, even when employed to restrain hæmor-

rhage, has caused a new hæmorrhage at the time of the separation of the sloughs; so that even this remedy must not be employed without a due consideration of the dangers which await it. Chap. VIII.

The preparations of mercury seem to be particularly injurious to some cases of hæmophilia; and the physician should be on his guard when prescribing this remedy. But, on the other hand, it must be remembered that mercury is usually given to bleeders with no ill effects.[1]

This will be the most convenient place to discuss the question of the propriety of any surgical interference with the knife. In every case on record, where amputation has been done, or large artery tied, or any of the great operations of surgery performed, as, for example, lithotomy, the patient has died either of the bleeding caused by the operation itself, or of the bleeding for the relief of which the operation was undertaken: in this latter case, the wound of the operation has, in many cases, been a source of fresh hæmorrhage, and thus hastened the fatal ending. With these facts in view, the question of a cutting operation becomes of the last importance. I am disposed to regard the following rule as imperative: that no cutting operation be undertaken, unless the patient's life be in danger for want of that particular operation, and for which no other, not involving the use of the knife, can be substituted. The resources of conservative surgery should be strained to

[1] I have been assured that the employment of the perchloride of mercury in small doses has been followed by the happiest results in the treatment of hæmorrhage in hæmophilia.

CHAP. VIII. the utmost before any question of amputation be raised: and it is very much to be feared that Mr. Marshall's most ingenious suggestion for performing small amputations by means of the electric cautery would prove unavailing in practice, if the separation of the sloughs caused by the heat became a new source of bleeding.

Tumours may be removed and fistulæ treated by following a plan lately revived by Mr. Henry Lee:[1] the part to be divided is gradually separated by the pressure of an elastic thread.

When a stone has been detected in the bladder, a fair trial might be given to the solvent method, as carried out by Dr. Roberts:[2] and this would be especially adapted to children in whom uric acid calculi are so common. In the adult, lithotrity appears preferable to lithotomy.

The removal of a tooth ought rarely to be sanctioned. Several circumstances unite to make hæmorrhage from the alveolus peculiarly uncontrollable. The divided vessels in the bone cannot fall together; and before the bleeding can cease, they must be plugged by a thrombus, which, because the vessels cannot contract, is indisposed to form: then the warmth of the mouth, and the suction which the patient involuntarily exerts, favour the continuance of the bleeding. The employment of pressure can only be partial and inadequate; astringents can only be imperfectly applied to some parts of the bleeding surface; this is especially true of caustics and the red-

[1] Henry Lee, *Proceedings of the Royal Med.-chir. Soc.* vol. vi. p. 293. Paper read June 14, 1870.

[2] William Roberts, *A Practical Treatise on Urinary and Renal Diseases*, London, 1865, p. 233.

hot iron, which must besides lose a great deal of its heat before it can be properly got into the alveolus, unless indeed the electric cautery be used. All these circumstances render the taking out of a tooth especially dangerous; and a great number of the fatal and alarming hæmorrhages on record have been due to this trifling operation. Under these circumstances, it will be granted that a practitioner would, as a rule, be worthy of blame in allowing a tooth to be removed.[1] Chap. VIII.

i. When persons, the subjects of hæmophilia, meet with an injury, it is desirable at once to use energetic measures for arresting the hæmorrhage without waiting for further symptoms: the earlier the treatment is begun, the greater are the chances of success. Compression seems to offer the best method of resisting the bleeding; and it seems advisable to try this first before resorting to any other means. The wound should be carefully cleaned, any bleeding points secured, the raw surface may, or may not, be touched with nitrate of silver, and then pressure applied with a cork and bullet, or graduated compress. It is needless to add that many modifications of the principle of applying pressure will be suggested by various cases as they occur: they are likely enough indeed to tax the ingenuity of the surgeon to the utmost. The easy production of ecchymoses must be borne in mind, while applying the pressure, even with a bandage, as well as the tendency to slough.

In one or two cases, the compression of the artery

[1] In a case recorded by Miller (*Edinburgh Medical Journal*, 1856, Jan. p. 638) the bleeding from the gum did not cease till the tooth was taken out.

CHAP. VIII. leading to the injured spot has succeeded in checking the bleeding. Ligature of the artery is inadmissible: in those cases in which it has been done, death has invariably followed.

Of styptics, Fordyce's saying still holds good.[1] All the astringent remedies in the *Materia Medica* seem to have been employed. Very often many drugs have been used without any success until the bleeding has lasted so long that it has stopped of itself. In this case a great astringent virtue is ascribed to the drug last employed. The nitrate of silver, tannin, and the perchloride of iron seem to be the local remedies that offer the greatest chance of success. The use of ice may be advantageously combined with compression. The hot iron is of very doubtful advantage, since when the sloughs separate, the bleeding usually begins again. Sometimes, however, it has succeeded; and it seems proper to use it as a last resource, and where it is impossible to use compression properly.

Should a leech have been applied, and the bleeding become dangerous, it is best arrested by the use of the nitrate of silver; or, if this fail, as it commonly does, by the employment of a hare-lip pin and figure-of-8 suture.

The hæmorrhage which occurs after the removal of a tooth is very difficult to manage. The most successful treatment seems to be a careful plugging of the alveolus with a graduated compress soaked in the perchloride of iron, or a thorough application of the nitrate

[1] "Styptica qualiacumque pro nihilo erant." Fordyce, *Fragmenta*, p. 41.

of silver, or the electric cautery, to the interior of the alveolus, not merely touching the bleeding surface but allowing the caustic to press for a few seconds on the part as it passes over it; this also to be followed by plugging.[1] When the bleeding has ceased, the patient must be fed on slops for several days after, as the act of mastication may easily bring on the bleeding again.

ii. The local treatment of the spontaneous hæmorrhages depends chiefly on the place of bleeding, whether accessible or not. Ice may be used locally, as to the loins in hæmaturia, or epigastrium in hæmatemesis. In epistaxis, gallic acid or tannin may be snuffed up into the nose, iced water injected, or the posterior and anterior nares plugged. Bleeding from the gums should be treated with tannin or alum washes, and ice allowed to dissolve in the mouth, while the patient is warned against sucking. In bleeding from the rectum, ice introduced within the bowel seems to be a good plan of treatment.

As to the constitutional treatment of the hæmorrhages: it does not in all cases seem advisable to try immediately to check the hæmorrhage when it is spontaneous, and has been preceded by symptoms of congestion, and the other prodromata described above. In these cases, if the bleedings be arrested too early, harm may be done.

During the prodromata much may often be done to ward off the bleeding. The patient should be allowed only a vegetable diet, wine and meat being rigorously excluded, and two or three purgative doses given, one

[1] The tooth itself is used by some as a plug.

CHAP. VIII. after another. In this stage some[1] have recommended phlebotomy: the terrible danger attending its use must deter every careful practitioner from such an idea. In spontaneous hæmorrhages it is well to continue the restricted diet and purgatives for some time after the bleeding has begun. The saline aperients seem to be most suitable; for although a wider experience has not met with many examples of the surprising results described by Otto[2] as obtained with the sulphate of soda, yet this salt, or the sulphate of magnesia, as recommended by Fordyce,[3] should be preferred.

[1] Consbruch, (Hufeland's *Journal*, Bd. xxx. Stück v. p. 117) the warmest advocate of prophylactic bleedings, confesses that in his cases six weeks of the strongest pressure was necessary to check the bleeding after a little scarification: and after this the arm was swollen and blue. Wachsmuth (*op. cit.* p. 51.) allows phlebotomy in adults only. Whatever may be the benefits of phlebotomy, the fact remains, that death has very frequently followed its employment, and the danger of this more than counterbalances any probable good.

[2] Otto, *Medical Repository*, New York, 1803, vol. vi. p. 2. "A few years since the sulphate of soda was accidentally found to be completely curative of the hemorrhages I have described. An ordinary purging dose, administered two or three days in succession, generally stops them; and, by a more frequent repetition, is certain of producing this effect. The cases in which the most powerful, and apparently the most appropriate remedies have been used in vain, and those in which this mode of treatment has been attended with success, are so numerous, that no doubt can exist of the efficacy of this prescription. The persons who are subject to this hemorrhagic idiosyncrasy, speak of it with the greatest confidence."

[3] Fordyce, *Fragmenta*, p. 42. The use of this remedy was suggested to him by Frederick Hoffman.

Should the bleeding, whether traumatic or spontaneous, continue, it is necessary to use internal remedies with a view of checking the flow. Nearly all the styptics of the *Materia Medica* have been used internally: acetate of lead, alum, the mineral acids, oil of turpentine, tannin, and gallic acid, with more or less success, or with none at all. Small doses of tartarised antimony and ipecacuan have been given so as to nauseate the patient, the object being to diminish the blood pressure, and thus allow the blood to coagulate. Strychnine, kreosote, arnica, opium, and the tincture or extract of the common shepherd's purse have all been recommended.

The ergot seems to have been of use in several cases of traumatic or spontaneous hæmorrhages. It should be given frequently, every hour or half hour in doses of 5 to 10 grains; or the tincture may be preferred, in doses of ten to fifteen minims. It must not be forgotten that some of the patients to whom the ergot was given with such success, had already suffered great loss of blood: and it is just possible that the time of the administration of the ergot corresponded with the natural termination of the hæmorrhage.

Amidst such conflicting testimony it is difficult to make out what is really the best plan to be pursued. If it could be shown that any of the drugs mentioned above had done harm to the patient, it would be certainly better to abstain from all active interference. To do this would demand a courage which few possess: but I do not think that the patients would be thereby injured. Were I called upon to treat a case of severe hæmorrhage, spontaneous or traumatic, I should prefer to use the tincture of the perchloride of iron in doses

CHAP. VIII. of 30 to 40 minims every 2 hours, taking care at the same time to purge the patient with the sulphate of soda or magnesia: this last would of course be inappropriate in cases of bleeding from the intestines. Did the hæmorrhage continue, the ergot might be employed, or the gallic acid, or any of the other means, as a last resort. When every other means has been employed, and the patient is in imminent danger of dying of loss of blood, transfusion seems to be the only refuge: it has been performed but once, in Mr. Lane's case: on the 6th day after the operation for squint, 10 or 12 oz. of blood were injected into the vein at the bend of the elbow: the benefit was not immediate, but in a few hours the boy, from lying as if dead, sat up and drank a glass of wine from his own hand.[1]

During the early part of a spontaneous hæmorrhage, the diet, as has already been remarked, should be restricted. When, however, the patient grows weak from loss of blood, the most nourishing food that can be obtained should be given, such as the strongest beef-tea, and soups. The use of wine must be regulated by the state of the pulse. Reynell Coates[2] attributes the recovery of one of his patients to the generous diet, and a free use of tincture of opium: in this case it is remarkable that the bleeding used to stop after meals,

[1] Lane, *Lancet*, 1840, Oct. p. 186. Panum finds that transfusion is just as efficacious when whipped blood is employed, as when the blood is injected immediately into the veins. See his Experimentelle Untersuchungen über die Transfusion, in Virchow's *Archiv f. path. Anat.* Bd. xxvii. p. 240.

[2] Reynell Coates, *North American Medical and Surgical Journal*, 1828, vol. vi. pp. 43-45.

especially after a warm breakfast. The blood apparently was drawn into the belly by the digestive flux, leaving the external parts anæmic, and the bleeding in them being thus arrested for a short time.

iii. As to the treatment between the attacks of hæmorrhage: this must be purely empirical, as the pathology of the disease is unknown. The tincture of the perchloride of iron has, in my experience, been of the greatest service: after its use, patients have become less subject to spontaneous bleedings, and wounds have been followed by hæmorrhage that was scarcely more than natural. Mr. Christopher Heath has made the same observation.[1]

Other preparations of iron do not seem to be so efficacious. With the perchloride may be given the cod-liver oil, if there be any wasting; or the two may be given alternately, for six weeks at a time. From these two medicines more may be expected than from other drugs. They should not, however, be continued when there are any signs of plethora: they would then do more harm than good.

Much may be done by hygienic treatment. Cold bathing is of great use, and is well borne. The patients should use a cold sponge bath every morning; and in the summer, sea-bathing, or chalybeate baths. In England, the waters of Harrowgate may be recommended; especially as the air there is dry and bracing.

The patients should always be warmly clothed; flannel or Scotch wool should be worn from the wrists to the ankles. They are almost always chilly, and suffer

[1] Christopher Heath, *British Medical Journal*, 1868, vol. i. p. 25.

CHAP. VIII. much from changes of temperature. Exposure to cold and damp is often followed by bleedings, but more frequently by swollen joints.

The diet of these patients should be nitrogenous, but unstimulating. Meat may be taken twice a day: there seems no especial reason why the white meats should be chosen; mutton and beef, properly cooked, may be allowed. Into the diet of children, of course, milk must enter in large proportion. It would seem best altogether to forbid wine, unless the patient be very weakly: it often causes inconvenient flushing of the face, even when taken in small quantity. Dequevauviller says that, in a case of Herrgott's, every time a little wine was taken a hæmorrhage followed.[1]

Cold and damp climates and situations should be carefully avoided, especially when the joint swelling is a feature of the case. Against damp houses there is scarcely needed any caution. During the winter, these patients should be sent to a warm and dry climate, such as Cannes in the south of France, or Nice, Egypt or Algiers. They should leave England at the end of October, and not return till May. During the summer,

[1] Dequevauviller, *De la disposition aux hémorrhagies*, Thèse de Paris, 1844, No. 87. p. 36. There is also another case which Grandidier quotes (*op. cit.* p. 134.) to show the injurious effects of port wine. It is the case recorded by Walker in Duncan's *Annals of Medicine for* 1797, vol. ii. p. 231, and had Grandidier seen this original, he would at once have recognised that the case was not one of hæmophilia at all, but was only a temporary hæmorrhagic diathesis, arising during the progress of whooping cough. On the other hand, Higginbotham found great advantage from the daily use of double stout (*St. Petersburger medic. Zeitschrift*, Bd. xvi. p. 113.)

they receive great benefit from the high and dry parts of northern Scotland, where they should not stay after September. The advantage to be expected from a warm climate is well set forth in one of Dequevauviller's cases, where a feeble boy of 14, subject to continual epistaxis while living in Paris, was, after two years of fruitless treatment, sent to Nice: in this warm and dry air the hæmorrhage ceased, and the general health greatly improved. In two years he returned to Paris, and three months had scarcely gone by, when the epistaxis came back with all the old severity. A warm climate is more imperatively demanded when the tendency to swellings of the joint is very marked; for the swellings are commonly excited by exposure to damp and cold.

iv. The treatment of the swellings of the joints must be conducted on ordinary surgical principles. During the first few days of effusion, cold or warm applications should be used, whichever is more grateful to the patient. Later on, after the first violence of the attack has subsided, the limb may be put into a splint, or cased in starch or plaster of Paris. Blisters are sometimes very useful in this stage. When the synovial fluid is but little in excess of nature, I have seen great advantage from strapping. In prophylaxis of the joint affection, a warm and dry climate, as mentioned above, is essential.

CHAPTER IX.

HYGIENE AND SOCIAL RELATIONS OF HÆMOPHILIA.

The practitioner whose duty it is to attend the families in whom this disease exists, will often be called upon to give his opinion as to the advisability of certain steps: and, in some cases, he may have it in his power to bar the entrance of so terrible a disease into previously healthy families.

Should the mother in a bleeder family suckle her own children? The question has been answered in different ways by various writers who have considered the subject. I do not feel inclined to attach much importance to it; it would perhaps be safer, in those cases where it may be had, to recommend a wet nurse.

The midwife should take special care that the cord is rightly tied; and also should watch the falling off of the stump, at which time hæmorrhage is most likely to happen.

Hæmophilia seems to be more common among the Jews than among other races or nations of men. On medical grounds, circumcision should certainly be forbidden, since the danger of such an operation would be very great. I am also informed that dispensation from this ceremony can be obtained.

The risk of vaccination is exceeding small: in only two cases has anything untoward ever followed; in nearly all the others, it is expressly mentioned that the

vaccine vesicle ran its usual course. Nevertheless, the inoculation should be done by scarification, and not by incision, since the former seems to be less dangerous.

Those who have charge of children, who are the subjects of this disease, should be admonished of the evil consequences that might follow any harsh treatment of the boys. Almost every kind of bodily punishment must be forbidden. And in their occupations and amusements, great care is necessary to guard against any mischance. Cricket and football are plainly unsuitable. Some of the occupations of the gymnasium, and boating, do not, however, seem to be hurtful. Riding may be allowed, if not followed by hæmaturia. But all these permissions depend a good deal on the state of the joints. If the knee or ankle be very liable to swell, nearly all these amusements must be given up, and the boys allowed to walk only, and that carefully.

As the boys grow up, the choice of a trade or profession becomes a matter of considerable importance. Among the artizan class, it is difficult to choose a business in which there does not appear a likelihood of almost daily wounds. Wachsmuth recommends the occupation of an agricultural labourer;[1] but this surely is as dangerous as any other, and the exposure to the changes of weather is not likely to be favourable to the joints. In large towns, the trade of a compositor might be recommended. Among the lower middle class, the business of a clerk, either in the public services or in trade, might be chosen. For others, the ecclesiastical

[1] Wachsmuth, *op. cit.* p. 58.

CHAP. IX. state,[1] the profession of a schoolmaster, the law, and especially the arts, whether architecture, painting, or music, offer very suitable employments. Neither does the medical profession seem to me unfavourable. The military or naval professions must certainly be avoided. In Germany, hæmophilia is a disqualification for the *Landwehr*. Field sports of all kinds, except the easier kinds of fishing, should be forbidden. The recoil of the fowling piece or rifle causes large ecchymoses, and the exposure to cold and damp is unfavourable for the swellings of the joints.

One very important social point is the question of marriage. Should a bleeder, or one of a bleeder family, be allowed to marry? I think that if the person himself be a bleeder, the question of marriage ought not to be entertained. His sons may possibly escape the disease, but it is almost sure to reappear in his daughters' sons. The prospect of the certainty of so dreadful an entail of disease must repel every right thinking person from such a step, even at so great a sacrifice to himself; and it seems only necessary for the facts to be known to prevent such marriages among the better classes.[2]

But in the case where a person belongs to a bleeder family, but is not himself the subject of the disease,

[1] Especially in those parts of the Church where celibacy is enforced; for this would remove all prospect of transmitting the disease by marriage. I do not know, however, if this disease would be considered a disqualification for Orders.

[2] I say in the better classes: for the artizan class are so ruled by their passions, that no moral restraints would ever be allowed to interfere with the gratification of a lust: the law must stop such contracts.

should marriage be allowed ?[1] I think not : supposing the candidate to be a man, the disease may possibly be passed on to his children, or grandchildren ;[2] and in the case of a woman, the disease is nearly certain to reappear in her sons : few circumstances with respect to hæmophilia are better made out than this. CHAP. IX.

The physician, whose advice is asked on this subject, should be on his guard not to be deceived by any appearance of freedom from hæmophilia in the women : they may seem perfectly well and free from any trace of the complaint, and yet the disease will certainly reappear in their sons. A sadder heritage of disease could scarcely be entailed : and a person entering upon marriage with a knowledge of all these facts would indeed be open to great blame.

It is plain that, if hæmophilia were rather more common, it would afford a good many cases of dispute in the courts of law. In Germany, it has already begun its medico-legal career, and the same may happen in this country at any moment. Should death take place from hæmorrhage after a slight wound, an accusation of manslaughter might at once be brought ; and

[1] It is surprising that Grandidier should disregard the possibility of hæmophilia being transmitted through the daughters of bleeders : he even seems to allow of the marriage of bleeders themselves ; and (*op. cit.* p. 19.) says that if a man from a bleeder family at Tenna married a woman from a healthy family, the disease did not appear in their offspring. This is certainly not the case in the history of English families.

[2] In one of Krimer's patients, the uncle was a bleeder, the father not ; yet the disease appeared in the sons and grandsons : See Horn's *Archiv*, 1820, Mai-Juni, p. 409. The case of Day (p. 10.) is similar.

 the success of the accusation would depend a great deal upon the prisoner's knowledge or ignorance on the subject of the dead man's peculiarity. If he were ignorant of the disposition to abundant hæmorrhage, he could scarcely be severely punished; while if the wound were inflicted with a full knowledge of the probable consequences, the charge of murder might be substantiated.

CHAPTER X.

ON CERTAIN HÆMORRHAGIC DIATHESES IN WOMEN.

A chronic hæmorrhagic diathesis is not unfrequently seen in women; but there are few cases on record,[1] for those seem to have been chiefly chosen for publication which exhibited the symptom of hæmatidrosis.[2] This

[1] I have published two cases of a chronic hæmorrhagic diathesis in women in the *Medical Times and Gazette*, 1871, vol. ii. p. 672.

[2] The following are some of the most important cases:

Philosophical Transactions, 1705, vol. xxiv. No. 303, p. 2114 (wrongly paged 2144.) Epistola Antonii Mesaporiti, M. C., Genuensis, ad Cl. Antonium Vallesnerium.

Patrick Murray, *Edinburgh Medical Essays and Observations*, 1737, vol. ii. Art. xx. 2nd edit. p. 306.

Boerhaave, in van Swieten's *Comment.* t. iv. § 1286.

Boivin, *Journal de médecine.* Quoted in *Dictionnaire des Sciences méd.* t. iv. p. 188. *Cas rares.*

Caizergues, *Annales cliniques de Montpellier*, 1814, nov. Quoted by Parrot.

Chauffard, *Transactions méd.* 1830, t. ii. p. 134.

Gendrin, *Traité philos. de Méd. pratique*, Paris, 1838, t. i. p. 285.

Hyde Salter, *Medical Times and Gazette*, 1856, vol. i. p. 253.

Magnus Huss, *Arch. gén. de Méd.* 1857, vol. ii. p. 165. The article is also contained in full in *Zeitschrift f. klin. Med.* Bd. viii. p. 347; and, without the commentary, in *Allgem. med. Central-Zeitung*, 1856, pp. 766 and 774.

Jules Parrot, *Gazette hebdom.* 1859, t. vi. p. 634.

T. K. Chambers, *Lancet*, 1861, vol. i. p. 207.

A. von Franque, *Würzburger med. Zeitschrift*, 1863, Bd. iv. p. 73.

Higginbotham, *St. Petersburger med. Zeitschrift*, 1869, Bd. xvi. p. 111.

There is also a case by Hoffman, *Omnia Opera*, Genevæ,

CHAP. X. last symptom, being thought a marvel, has drawn a good deal of attention; but I wish to point out that it is only part of a group of symptoms, a part of a general disposition to bleed, usually attended by indications of a grave nervous lesion. It will be seen at once that several distinct diseases are included in the genus of chronic hæmorrhagic diathesis: but sufficient attention has not yet been paid to this group of symptoms to allow any division into species to be made.

i. Ætiology. In all the cases but one, no symptoms of hæmorrhage appeared before puberty. In Parrot's case the hæmorrhages appeared about the age of 6 years: under the influence of anger, the tears were coloured with blood, and blood also appeared at various parts of the skin. In Boerhaave's case, which is the next earliest, symptoms appeared in the twelfth year, with the first menstruation. Boivin's case gives the latest age; for the woman was perfectly well up to the 28th year of her life.

In most of the cases, nothing is said of the previous habits and constitution of the patient. In 4 cases it is stated that the general health was very good up to time of the setting in of the diathesis. In three cases it is stated that the patients were of an irritable disposition.

1740, t. iii. sect. i. cap. v. p. 63; and by Stahl, *De viis mensium insol.* cap. v.; and by Le Cat, *Journal de médecine*, 1764, t. xx. avril, p. 326, and a number of cases are referred to by Haller, *Elem. Phys.* lib. xxviii. § iii. p. 157; but most of them are either only temporary hæmorrhagic diathesis, or are too meagre in detail to be serviceable. There are also many cases quoted by Latour, *Histoire philos. et méd. des Hémorrhagies*, Paris, 1828, t. i. p. 226.

In seven of these cases, the first hæmorrhage was preceded by a violent moral emotion, which, in four cases, was brought about by some external injury. In two, the hæmorrhages first appeared while the catamenia were flowing.

ii. Symptoms. In 5 cases, the exciting cause of the hæmorrhages could be traced to mental emotion. In Huss' case, the patient could even bring them on at will, by firmly directing her attention to the part. In my own two cases, the patients told me that they had never observed hæmorrhage to follow mental emotion.

Traumatic hæmorrhages have only been noticed in Higginbotham's and my own two cases. In Hyde Salter's and Huss' cases, spontaneous, and sometimes traumatic, ecchymoses were noticed. In Huss' and Patrick Murray's, wounds were not followed by excessive bleeding; but in all the other cases nothing is said on the subject.

The spontaneous hæmorrhages may come from all parts of the body; the mucous membranes, or skin; and in the latter case, the name of hæmatidrosis is given to the symptoms.[1] The bleedings may occur from nearly every mucous membrane; the nose, the mouth, and the uterus are the most common sources of blood; rarely is hæmaturia seen. Very often the hæmorrhage

[1] I am compelled to treat the subject of hæmatidrosis superficially: the limits of this work will not allow as full a discussion of this symptom as its interest demands; and for a philosophical account of nearly all that is known of this phænomenon the reader must consult Gendrin's *Traité philosophique de Médecine pratique*, Paris, 1838, t. i. p. 276; and Jules Parrot's articles in the *Gaz. hebd.* for 1859, beginning at p. 633.

CHAP. X. chiefly occurs from only two points; such as the nose and uterus; or the stomach and the skin.

Bleeding may take place from any part of the skin: in Boivin's case it is said that there was no part of the skin which had not yielded blood. In the others the blood has issued from parts of the skin which are the most thin and delicate, and which perspire more readily; thus bleedings have been most frequently seen from the face, the neck, the axillæ, the front of the chest, the inside of the thighs and arms, and the skin by the sides of the nails. Sometimes the blood comes from the eyelids, conjunctivæ, and ears; or from the hands and feet; or from the hairy scalp.

The skin from which the blood flows is usually quite natural; and when the hæmorrhage has ceased, no traces are left behind. In most of the cases, a pruritus and hyperæmia, together with some swelling and slight sense of pain, precede the flow of blood. Huss examined the bleeding surface of the scalp with the aid of a lens, and found the blood arise around the root of each hair, and form a little point of blood through the centre of which the hair passed: this point increased, and became a drop, which, uniting with other drops similarly formed, ran off. Observers are agreed that the blood escapes in other parts, which are free from hairs, from the orifices of the sweat glands; and Parrot thinks that in all cases the flow of blood takes place from the sweat glands only.

The fluid which escapes from the skin contains red corpuscles: this fact has been determined by Huss, Chambers, Parrot, and von Franque. In Chambers' case the blood from the skin did not form rouleaux,

while that from the finger did so quite naturally. Huss found in the blood from the scalp no alteration of the red corpuscles in shape, but they did not form rouleaux; there was a complete absence of the white. The blood was always of a bright red colour, like arterial blood. In Patrick Murray's old case, the blood was no higher coloured, nor of thicker consistence than water in which flesh has been washed.

In Murray's and Higginbotham's cases, the quantity of blood lost was fabulous. In the first case, half a pound of blood was lost from the nose every day for two years, exclusive of what was lost from the uterus, stomach, and the skin. In the second, menorrhagia lasted 472 days, the patient losing half a pound of blood daily; so that, altogether, 2800 to 3000 ounces must have been voided. As a rule, the amount of blood lost, although considerable, is not nearly so great as this; enough is lost, however, to cause great anæmia.

The presence or absence of menstruation seems to have no influence on the disease. Out of the 13 cases, the references to which I have given in the note to p. 129, the menses remained unaltered in 6; they were irregular, sometimes profuse, sometimes absent, in 2; their appearance several times is mentioned in 2 cases, but no further details given; in only one case were they entirely absent; and in the remaining two, there was menorrhagia. In my own two cases, menorrhagia was a prominent symptom.

In 7 cases, in which the hæmatidrosis was the most prominent symptom, there have been nervous attacks about the nature of which considerable doubt is usually

CHAP. X.

expressed. They are looked upon as either epileptic or hysterical. In all the cases, except Chambers', there appear to have been general convulsions. In Parrot's case, the patient became almost maniacal. In von Franque's case, the disease was thought, by some of the physicians who saw the patient, to be chorea.

iii. Duration. In 8 out of the 13 cases, the disease was in progress at the time that the authors wrote their description. In Gendrin's case, the patient married, became pregnant, and lost her troubles; but the hæmorrhagic diathesis in this case was not very pronounced. In Higginbotham's case it is not quite certain if the patient recovered or not. In the other three cases, the symptoms had disappeared. In my own two cases, the disease had lasted certainly 12 years in one case, and 4 in the other. The disease does not seem to have any influence in shortening life: in Boivin's and Murray's cases, where great quantities of blood were daily lost, the patient continued to live many years.

iv. Pathology. I am not aware of any records of a *post mortem* examination of a patient suffering from a hæmorrhagic diathesis of this kind. There seems to be no appreciable disease of the blood: it is not wanting in fibrin, for it coagulates quickly and firmly; nor are the corpuscles altered. It does not seem to be any way related to menstruation, since in many of the cases, the catamenia remain unaltered throughout the progress of the malady.

It is a matter of almost daily observation that women are far more liable than men to spontaneous hæmorrhages of all kinds. In women, a spontaneous hæmor-

rhage is a natural phænomenon every month; and at every catamenial period, there appears to be a greater disposition in other parts of the body, remote from the uterus, to bleed upon slight causes: in many of the cases of hæmorrhagic diathesis, the bleedings have first occurred at the monthly period.[1]

In many of these cases, the exciting cause, not only of single hæmorrhages, but even of the hæmorrhagic diathesis, appears to have been a violent mental emotion; in some of them, again, coinciding with the flow of the catamenia. That a temporary hæmorrhagic diathesis may be caused by mental emotion is shown by the observation of Lordat: a woman of bad life, and extremely irascible character, was seized by the police and taken to prison. She became furiously angry; and shortly after, suffered a hæmorrhage from the nose and mouth; and an eruption of purpuric spots, which covered the whole body; the largest of these spots were an inch in diameter.[2] In women, the emotions are under little control: diseases, caused by the emotions, as hysteria, are common: and there is good reason, in the cases mentioned above, for the belief that the hæmorrhagic diathesis was established as sequence to the violent moral emotion. In other cases, the symptoms have been complicated by the appearance of nervous phænomena, general convulsions;

[1] The reader will find the references to many of these cases in Jules Parrot's last article.

[2] Lordat, *Traité des hémorragies*, Paris, 1808, p. 84. There are also two old cases, frequently quoted, by Severinus and Florentinus Leudanus, of two nuns, who, being by chance greatly alarmed, suffered an exudation of blood from the skin and other parts.

CHAP. X. so that it does not seem impossible that the disease may arise from some lesion of the central nervous system, implicating as well the vaso-motor nerves, the paralysis of which may be the cause of the hæmorrhages, by relaxing the walls of the blood vessels, and thus allowing their rupture by an amount of blood pressure far less than in the natural state. In some cases, the hæmorrhage is limited to one side of the body.

Hæmatidrosis is but a part of the symptoms of a hæmorrhagic diathesis. In all the cases in which this bloody sweat has occurred, except Chauffard's, hæmorrhage, usually abundant, has also occurred from the mucous membranes as well.

v. Diagnosis. At first sight, the diagnosis may not be easy. The resemblance to hæmophilia may be very great: in my own two cases, it was almost complete. In making the diagnosis, the hereditary and congenital character of hæmophilia must be kept in mind; if no symptoms of a disposition to hæmorrhage have appeared until after puberty, the case cannot be one of hæmophilia: further, the rejection of the diagnosis of hæmophilia will be strengthened, if there be no trace of the presence of this disease in the kinsmen: and especially if the women have borne sons, free from hæmophilia; hæmophilia being nearly sure to reappear in the sons of a woman, who is herself the subject of hæmophilia. If, on the contrary, the women spring of a bleeder family, with symptoms appearing in childhood, the case must clearly be referred to hæmophilia. Hæmophilia is almost the only disease with which these hæmorrhagic diatheses could be confounded.

The acute hæmorrhagic diatheses are excluded by the short course which they run. The hæmorrhagic diathesis of leucæmia will be recognised by the increase of leucocytes in the blood, and the enlargement of the spleen or lymphatic glands.

vi. Treatment seems to have little influence over the hæmorrhagic diathesis. In most of the cases, the drugs employed seem to have in no way influenced the course of the disease. In my own two cases there was certainly some relief from the local symptoms after the employment of large doses of the tincture of the perchloride of iron. A fair trial might also be given to the secale cornutum and oil of turpentine.

For the alleviation of the nervous symptoms, opium or chloral may be given in moderate doses; but care must be exercised in their administration, as the patients are very likely to acquire a habit of employing these remedies in excess. The inhalation of chloroform vapour seems to be of great use in checking the convulsions, which must, of course, be distressing to the bystanders.

CHAPTER XI.

LITERATURE OF HÆMOPHILIA.

CHAP. XI. Hæmophilia is shortly described in the text books by Erichsen, Miller, Tanner, Holmes, Wood, Austin Flint, Gross, Rilliet and Barthez, Bouchut, Grisolle, Follin, Monneret, Gintrac, Schönlein, Canstatt, v. Pitha and Billroth, Felix v. Niemeyer, &c. The descriptions are none of them complete. There is a good account of the disease by Virchow in the first volume of his *Handbuch*.

The following monographs have also appeared:

James Miller, *Monthly Journal*, 1842, July, p. 567. This paper deals chiefly with the treatment.

Nasse, *Correspondenzblatt rheinisch-westphäl. Aerzte*, 1845. No. 14.

Schneider, Henke's *Zeitschrift f. d. Staatsarzneik.*, 1847, Bd. liii. p. 1.

Lange, *Medicinische Zeitung (Vereins)*, 1847, p. 124. Ueber geographische Verbreitung der Bluterkrankheit.

Lange, Oppenheim's *Zeitschrift*, 1851, Bd. xlv. p. 145.

Wachsmuth, *Die Bluterkrankheit*, Magdeburg, 1849: this first appeared in *Zeitschrift des deutschen Chirurgenvereins*, Bd. iii. p. 459.

Bordmann, *De l'hémophilie*, Thèse présentée a la Faculté de Médecine de Strasbourg, 1851.

Grandidier, *Die Hämophilie oder die Bluterkrankheit*, Leipzig, 1855.

Grandidier, Schmidt's *Jahrbücher*, Bd. cxvii. p. 329. Bericht ueber die Hämophilie.

Laycock, *Medical Times and Gazette*, 1862, vol. i. p. 500.

The following cases have been arranged in alphabetical order, in geographical classes. Cases of mere hæmorrhagic diathesis have been rejected, whether of umbilical hæmorrhage, as the cases of Minot, Bowditch, Manley, Dubois, Mende, Beckhaus, &c., or of pseudo-hæmophilia, as those of Huss, Higginbotham, and some others. Cases, again, of a great hæmorrhage on one occasion only, have been omitted, such as those of Droste, Sturm, &c. Many cases, hitherto unnoticed, have been added to the list. CHAP. XI.

AMERICAN.

W. and S. Buel, **Transactions of the Physico-Medical Society of New York*, 1817, vol. i.: also in the *London Medical and Physical Journal*, vol. xl. p. 429; **Hamburger Magazin für die ausl. Lit.* Bd. iii. p. 449; **Gött. gel. Anz.* 1821, Stück xcii.; **Journal universel des sciences méd.* t. xiii. p. 349.

Reynell Coates, *North American Medical and Surgical Journal*, Philadelphia, 1828, vol. vi. p. 37: also in Kleinert's *Repertorium*, 1831, Heft. xi. p. 54; **Sammlung auser. Abhandl. f. prakt. Aerzte*, Bd. xxxvii.; **Journal des Progrès*, t. xiii. p. 61.

Gould, *Boston Medical and Surgical Journal*, 1857, vol. lvi. p. 500; also in *Medical Times and Gazette*, 1858, vol. i. p. 19. Only the genealogical tree of a certain family.

Hay, *New England Journal of Medicine and Surgery*, Boston, 1813, vol. ii. p. 221: also in *London Medical Repository*, 1815, vol. iii. p. 69; Meckel's *Archiv f. d. Phys.* 1816, Bd. ii. p. 138; *Hufeland's *Journal*, Bd. xli. Stück iii.; **Journal général*, t. lv. p. 418.

J. N. Hughes, **Transylvania Journal of Medicine*, voll. iv. and v.; also in *American Journal of Medical Science*, 1833, vol. xi. p. 542;

* The references marked with an asterisk are those which I have not myself verified.

CHAP. XI. *Archives gén. de Médecine*, 1833, oct. p. 278;[1] °Froriep's *Notizen*, 1838, Nr. 135.

Otto, *Medical Repository*, New York, 1803, vol. vi. p. 1: also in *London Medical and Physical Journal*, vol. xx. p. 69; *London Medical and Chirurgical Review*, vol. x. p. lvii.; Meckel's *Arch. f. d. Phys.* 1816, Bd. ii. p. 138; *Dictionnaire des Sciences médicales*, t. iv. p. 190; °*Gött. gel. Anz.* 1806, and 1809; °*Annales de littérature méd. étrangère*, t. vii. p. 163. The history is continued in the *Philadelphia Medical Museum*, 1805, vol. i. p. 286.

Tranéus, °*St. Louis Medical and Surgical Journal*, 1870, p. 535: also in Virchow and Hirsch's *Jahresbericht f.* 1870, Bd. ii. p. 286.

E. H. Smith, *Philadelphia Medical Museum*, 1805, vol. i. p. 284: a letter from Dr. E. H. Smith, of New York, to Benjamin Rush, M.D. dated April 9, 1794: at p. 288, the editor, Dr. J. R. Coxe, quotes 3 cases from Lowthorp's *Abridgment of the Philosophical Transactions*: also in *Sammlung auserlesener Abhandl. f. p. Aerzte*, Bd. xxii. p. 269.

BELGIAN.

Benavente, °*Annales de la Société de Méd. d'Anvers*, 1861, avril-mai: also in Canstatt's *Jahresbericht f.* 1861, Bd. iv. p. 230.

Gobée, °Oppenheim's *Zeitschrift*, Bd. xxvii.

DANISH.

P. St. Ursing, °*Journal for Medicin og Chirurgie*: also in Kleinert's *Repertorium*, 1838, April, p. 25; °*Med. Annal. der badischen Sanitätscomm.*, 1837, Bd. iii. Heft. iii.

DUTCH.

Tamme Beth, °*Specimen med. inaug. exhibens historiam haemorrhagiae insolitae e digitis dextrae manus et simul hereditariae*, Groning. 1829.

Donkersloot, *Nederlandsch Lancet*, 1850, p. 416.

[1] In the *Archives gén.*, the name Hughes has been changed into Hugues, apparently owing to the radical incapability of spelling a foreigner's name correctly, that the French possess: this way of spelling has been followed by the Germans, Virchow only excepted. (*Handb. d. spec. Path. u. Ther.* Bd. i. p. 264.)

EAST INDIAN.

Heymann, *Archiv f. path. Anat.* Bd. xvi. p. 182: also in °*Allgem. med. Central-Zeitung*, 1859, Nr. 42. A Mohammedan family at Palembang, in Java.

ENGLISH.

Allan, *Monthly Journal*, 1842, June, p. 501: also in °*Archives gén. de Méd.* 1843, 4e série, t. i. p. 83.

Babington, *Lancet*, 1865, vol. ii. p. 362: also in *Centralb. f. d. med. Wiss.* 1865, p. 864. Cases of hereditary epistaxis.

Blagden, *Med.-chir. Trans.*, vol. viii. p. 224.

Burns, *Lancet*, 1840, Dec. p. 404.

Buss, *Medical Times and Gazette*, 1868, vol. ii. p. 530.

Clay, *Medical Times*, 1846, Jan. 10, p. 293: also in °*Prager Vierteljahrschrift*, 1847, Bd. iii.; °Schmidt's *Jahrbücher*, 1847; °Oppenheim's *Zeitschrift*, Bd. xxxiii; *Gaz. méd.*, 1846, p. 568.

Clutterbuck, *Lancet*, 1826, April, p. 99.

Cochrane, *ibid.* 1842, April, p. 147: also in °Hufeland's *Journal*, Bd. xcv. Stück vi.; °Canstatt's *Jahresbericht*, 1842. After quoting several cases of obstinate hæmorrhage, describes the case of a man who nearly bled to death after the taking out of a tooth. The case of Walker, in Duncan's *Annals of Medicine* for 1797, vol. ii. p. 231, is one of a hæmorrhagic diathesis coming on and disappearing during an attack of whooping cough.

Cousins, *Medical Times and Gazette*, 1869, vol. ii. p. 277: also in Virchow and Hirsch's *Jahresbericht für* 1869, Bd. ii. p. 269.

Craig, *Edinburgh Journal of Medical Science*, 1826, vol. ii. p. 64: quoted also by Cochrane, who gives quite a wrong impression. Three cases are related, one only has any likelihood of belonging to the class of hæmorrhagic diathesis.

Davis, *Edinburgh Medical and Surgical Journal*, 1826, vol. xxv. p. 291: also in °Horn's *Archiv*, 1826, Mai; °Froriep's *Notizen*, 1826; °*Med. chirurg. Zeitung*, 1826, Bd. iv.

Druitt, *Provincial Medical and Surgical Journal*, 1845, April, p. 260.

Durham, *Guy's Hospital Reports*, 1868, vol. xiii. p. 489: also in Virchow and Hirsch's *Jahresbericht für* 1868, Bd. ii. p. 275.

CHAP. XI. Fordyce, *Fragmenta chirurgica et medica*, Lond. 1784, p. 41: also in °*Sammlung auser. Abh.* Bd. xi.

Hay, *Monthly Journal*, 1842, p. 264.

Christopher Heath, *British Medical Journal*, 1868, vol. i. p. 25: also in Virchow and Hirsch's *Jahresbericht für* 1868, Bd. ii. p. 275: and Schmidt's *Jahrbb.* Bd. cxxxix. p. 172.

Hooper, reported by Burns, *Lancet*, 1840, Dec. p. 405.

Hunt, *Provincial Medical Journal*, 1842, May, p. 143: also in °Canstatt's *Jahresbericht*, 1843, Bd. iv.

Kendrick, *London Medical Gazette*, 1830, p. 788. This case was described afterwards by Liston.

Lane, *Lancet*, 1840, Oct. p. 185: also in °*Arch. gén. de Méd.* 1841, févr. p. 234; °Froriep's *Notizen*, 1841, Nr. 394; °Canstatt's *Jahresbericht für* 1841, Bd. i.; °Kleinert's *Repertorium*, 1841; °Oppenheim's *Zeitschrift*, Bd. xxxvi. p. 581.

Wickham Legg, *St. Bartholomew's Hospital Reports*, 1871, vol. vii. p. 23.

Liston, *Lancet*, 1839, April, p. 137: also in °Hufeland's *Journal*, Bd. lxxxviii. Stück iv. p. 184.

London Medical and Physical Journal, vol. xl. p. 431.

Marshall, *Medical Times and Gazette*, 1870, vol. ii. p. 728.

John R. Miller, *Edinburgh Medical Journal*, 1856, Jan. p. 638.

Alexander Murray, *Edinburgh Medical and Surgical Journal*, 1826, vol. xxvi. p. 33.

Osborne, *Dublin Journal of Medical Science*, 1835, vol. vii. p. 32: also in °*Arch. gén.* 1835, juli, p. 385; °*Hamb. Magazin.* Bd. xxx. p. 131; °Froriep's *Notizen*, 1835, Oct.

Hyde Salter, *Med. Times and Gazette*, 1856, March, p. 253; also in °Canstatt's *Jahresbericht für* 1856, Bd. iv. The history of a woman with a hæmorrhagic diathesis is recorded, and a family of bleeders spoken of.

Smethurst, *Lancet*, 1841, Jan. p. 648. Two cases of a hæmorrhagic diathesis in women.

Taynton, *London Medical Gazette*, 1836, Jan. p. 659; also in °Froriep's *Notizen*, Bd. xlvii. Nr. 1036.

Wardrop, *On Blood letting*, London, 1835, p. 13.

Ward, *ibid*, p. 16.

Waterhouse, *British Medical Journal*, 1870, vol. i. p. 128, and vol. ii. p. 679.

West, *Provincial Medical Journal*, 1842, Sept. p. 438.

Wilmot, *Dublin Journal of Medical Science*, 1841, vol. xix. p. 234: also in °*London Medical Review*, 1841; °Oppenheim's *Zeitschrift*, Bd. xix. p. 431.

James Wilson, *Lectures on the Blood*, &c., London, 1819, p. 410.

James A. Wilson, M.D., reported by Lane, *Lancet*, 1840, Oct. p. 187.

FRENCH.

Bérard, quoted by Canstatt, *Handb. der med. Klinik*, 1843, Bd. i. p. 139.

Castan, °*Montpellier médical*, 1869, octobre: also in *Lyon médical*, 1869, t. iii. p. 464.

Crasner, *Gazette médicale de Paris*, t. iv. p. 599.

Delmas, °*Journal de Méd. de Bordeaux*, 1868, oct. p. 455: also in Virchow and Hirsch's *Jahresbericht für* 1868, Bd. ii. p. 275.

Dequevauviller, *De la disposition aux hémorrhagies*, etc. Thèse de Paris, 1844, No. 87: also in °*Journal de Chirurg.* par Malgaigne, 1844, juin, p. 164. Eight cases are recorded: only 3 are hæmophilia.

De Fleury, *Mémoires de la Société méd. chir. de Bordeaux*, 1866, t. i. p. 299.

Fournier, *Gazette des Hôpitaux*, 1851, p. 493: also in °Canstatt's *Jahresbericht f.* 1851, Bd. iv. p. 169.

Gavoy: see German cases.[1]

Gintrac, *Cours théorique et clinique de Pathologie*, Paris, 1853, t. iii. p. 110: also in *Mémoires de la Société méd.-chir. de Bordeaux*, 1866, t. i. p. 312.

Guépratte, °*Journal des connaiss. méd.-chir.* 1844, juin: also in Canstatt's *Jahresbericht für* 1844, Bd. iii. p. 291.

Laborie, *Gaz. des Hôp.* 1835, t. x. p. 178. This case is the same as that recorded by Lafargue.

Lafargue, *Revue méd.* 1835, t. iv. p. 89: also in °*Journ. hebdom. des progrès*, 1835, août; *Gaz. des Hôp.* 1835, t. ix. p. 410; °Schmidt's

[1] Since Germany has resumed the possession of Alsatia, I have thought it right to place the cases from Strassburg among the German observations.

CHAP. XI. *Jahrbb.* 1835, p. 57; °Oppenheim's *Zeitschrift*, Bd. i. p. 106; °Froriep's *Notizen*, 1835, Nr. 99.

Laveran, *Gaz. hebdom.* 1857, p. 621. Under the name of hæmophilia, a case of leucæmia with abundant epistaxis is described.

Lebert, *Archives gén. de Méd.* 1837, sept. p. 36: also in *Med. Chir. Review*, 1838, July, p. 226; °Froriep's *Notizen*, 1838, Nr. 119 and 120. Only 2 out of the 16 cases are new.

Poncet, *Lyon méd.* 1871, t. viii. pp. 785 and 798.

Victor Resal, *Quelques pages sur l'hémophylie*, Thèse de Paris, 1861: also in Canstatt's *Jahresbericht f.* 1861, Bd. iv. p. 228. Three cases of hæmophilia limited to spontaneous hæmorrhage.

Ritgen: see German cases.

Roux, °*Journal de Méd. et de Chir. prat.*, 1833, vol. viii. Quoted also by Lebert.

Saint Vel, *Union méd.* 1865, p. 110: also in Canstatt's *Jahresbericht f.* 1865, Bd. iv. p. 125; Schmidt's *Jahrbb.* Bd. cxxx. p. 27.

Schnepf, *Gaz. méd. de Paris*, 1855, p. 671.

Sentex, *Mémoires de la Société méd.-chir. de Bordeaux*, 1866, t. i. p. 311.

Tardieu, *Archives gén. de Méd.* 1841, févr. p. 185: also in °Oppenheim's *Zeitschrift*, Bd. xvii. Heft. iii. p. 367; °Schmidt's *Jahrbb.* Bd. xliii.

Thore, *Gaz. méd. de Paris*, 1856, p. 653: also in Schmidt's *Jahrbb.* Bd. xciv. p. 186.

Wolff: see German cases.

GERMAN.

Abt, °*Oesterr. Zeitschrift für prakt. Heilkunde*, 1855, Juni.

Assmann, *Die Hämophilie*, Diss. Inaug. Berol. 1869: an abstract in Virchow und Hirsch's *Jahresbericht f.* 1869, Bd. ii. p. 268.

Beier, *De haemophilia*, Diss. Inaug. Berol. 1864: an abstract in Canstatt's *Jahresbericht f.* 1864, Bd. iv. p. 158.

Besserer, °*Correspondenzblatt rhein.-westph. Aerzte*, 1845, Dec.: also in Canstatt's *Jahresbericht für* 1845, Bd. ii. p. 29.

Bicking, Hufeland's *Journal*, Bd. lxxxiv. Stück iv. p. 110.

v. Bippen, °*Bericht über die Vers. der Aerzte u. Naturforscher in Mainz*, 1843, *und in Bremen* 1844: quoted also by Heyland, °*Neue med. chir.*

Zeitung, 1844, Nr. 5; also in °*Gaz. méd. de Strasbourg*, 1843, p. 408.
Claudi, *Oesterr. med. Wochenschrift*, 1841, Nr. 19, p. 435.
Conradi, °*De morbo maculoso haemorrhagico*, Diss. Inaug. Götting. 1829.
Consbruch, Hufeland's *Journal*, Bd. xxx. Stück v. p. 116: also in *Journal gén. de Méd.* Paris, 1811, t. xli. p. 115; °*Bibl. méd.* t. xxxiii. p. 392; °*Annales de litt. méd. étrang.* t. xiv. p. 313.
Cramer, Caspar's *Wochenschrift*, 1835, p. 529.
Elsässer, Hufeland's *Journal*, Bd. lviii. Stück v. p. 89; Bd. lix. Stück iii. p. 109; Bd. lxvii. Stück v. p. 122; Bd. lxxvii. Stück v. p. 133: also in *Edinburgh Medical and Surgical Journal*, 1826, vol. xxv. p. 454; °*Nouvelle bibl. méd.* t. vii. p. 487; °*Bull. des Sciences méd.* t. xiii. p. 353.
Erdmann, °*Diss. de haemophilia*, Hal. 1844.
Escherich, ° *Wurtemb. med. Correspondenzblatt*, 1835, Bd. v. Nr. 19; also in Henke's *Zeitschrift f. d. Staatsarzneikunde*, 1847, Bd. liii. p. 18; Schmidt's *Jahrbb.* Bd. xiv. p. 25.
Finger, ° *Oesterr. Zeitschrift f. prakt. Heilk.* 1859, Bd. v.: also in Schmidt's *Jahrbb.* Bd. cvii. p. 301; Bd. cxvii. p. 330.
Fischer, °*Zeitschrift f. Chirurgie u. Geburtsh.* 1855, Bd. i.; also in Schmidt's *Jahrbb.* Bd. lxxxvii. p. 136.
Fränzel, *Medicinische Zeitung (Vereins)*, 1833, p. 164.
Gavoy, °*L'hémophilie ou diathèse hémorrhagique*, Thèse de Strasbourg, 1861: also in Canstatt's *Jahresbericht, f.* 1862, Bd. iv. p. 155.
Grandidier, °*Allgem. med. Zeitung*, 1837, Nr. 69.
Grandidier, °Holscher's *Annalen*, 1839, Bd. iv.: also in Schmidt's *Jahrbb.* Bd. xxviii. p. 170. The same family is also described in his °*De Disp. ad haemorrh. lethal. hereditaria*, Casselis, 1832.
Gröschner, Rust's *Magazin*, Bd. xxxvi. p. 397.
Henschel, Schmidt's *Jahrbb.* Bd. cxvii. p. 331.
Heyfelder, *Medicinische Zeitung (Vereins)*, 1833, p. 215.
Hopf, °*Die Hämophilie*, Würzburg, 1828.
Johannsen, °*Diss. de Haemorrhaphilia*, Kil. 1842.
Jungken, *Deutsche Klinik*, 1849, p. 55.
Kerksig, °*Sanitätsbericht der westphäl. Med. Coll. f.* 1843, p. 80.
Krimer, reported by Nasse, Horn's *Archiv*, 1820, Mai-Juni, p. 409.

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CHAP. XI. Kuhl, °*Opuscula medica, quaest. chirurg.*, 1834, pars xiii.: also in °Clarus und Radius *Beiträge*, 1836, Bd. ii.

Küster, Caspar's *Wochenschrift*, 1847, p. 282.

Lange, *Medicinische Zeitung (Vereins)*. 1846, p. 24.

Lemp, *De haemophilia nonnulla*, Diss. inaug. Berol., 1857: also in Schmidt's *Jahrbb.* Bd. cxvii. p. 330.

Löwe, *Zeitschrift des deutschen Chirurgenvereins*, Bd. i. p. 685.

Lucas, °*Sanitätsbericht des rhein. Med. Coll. f.* 1835: also in Froriep's *Notizen*, 1838, Nr. 121, p. 175.

Martin, °*Jenaische Annalen*, 1851, Bd. ix. p. 307.

°*Medicinische Ephemeriden*, Chemnitz, 1793, p. 267: also in *Gött. gel. Anz.* 1794, p. 279.

Medicinische Zeitung (Vereins), 1835, p. 27.

Meinel, °*Jenaische Annalen*, 1851, Bd. ix. p. 298.

Melicher, *Oesterr. medic. Wochenschrift*, 1844, Nr. 32, p. 869.

Miling, *Medicinische Zeitung (Vereins)*, 1844, p. 31.

Müller, °*De Morbis maculos. haemorrh.*, Gött., 1829.

Müller, J. J. Schmidt, °*De haemorrhoea*, Erlang. 1829.

Mutzenbecher, °*Diss. de haemorrhagicis*, Heidelberg, 1841.

Nasse, Horn's *Archiv*, 1820, Mai-Juni, p. 385.

Otte, *Ueber die Bluterkrankheit*, Leipzig, 1865: a reproduction of an inaugural Dissertation at Bonn in 1863: also in Schmidt's *Jahrbb.* Bd. cxxx. p. 25.

Quadrat, *Oesterr. med. Wochenschrift*, 1841, Nr. 33, p. 769. Two cases of doubtful hæmophilia.

Rave, °*Beobachtungen und Schlüsse aus der praktischen Arzneiwissenschaft*, 1798, Theil ii. p. 13.[1]

Reinert, *Ueber Hämophilie*, Diss. Inaug. Göttingen, 1869.

Rieken, *Neue Untersuchungen in Betreff der erblichen Neigung zu tödtlichen Blutungen*, Frankfurt, a.M. 1829: also in °*Annales de la Société de Méd. d'Anvers*: °*Bullet. de Thérapeutique*, t. xviii. p. 388.

Ritgen, °*Gaz. méd. de Strasbourg*, 1843, p. 408.

Rösch, °*Untersuchungen aus dem Gebiete der Heilwissenschaft*, Stuttg. 1837, Bd. i. p. 249.

1 Grandidier says that this case has not been mentioned, with reference to hæmophilia, before the publication of his monograph (p. 12.) It is, however, referred to by S. G. Vogel in his *Handb. der pract. Arzneywissenschaft*, Theil v. p. 14. after the cases from the *Medic. Ephem.* and Fordyce's.

Rüber, °*De dispos. ad haemorrh. lethal. hæreditaria,* Berol. 1832.

Salomon, Caspar's *Wochenschrift,* 1834, p. 97.

Sammlung. aus. Abh. Bd. xxii. p. 275.

Schliemann, °*Diss. de dispos. ad haemorrhagias perniciosas haereditaria,* Wirceb. 1831.

Schneider, of Aschersleben, Rust's *Magazin,* Bd. xxx. p. 463.

Schneider, of Offenburg, Schmidt's *Jahrbb.* Bd. xxiv. p. 354.

Schreier, °*Dresdner Zeitschrift f. Natur- und Heilkunde,* Bd. v. Heft. ii. p. 333: also in *Journal des Progrès,* 1828, vol. xi. p. 243; °*Bull. des Sci. méd.* t. xiii. p. 353.

Schrey, °*Diss. de Hæmophilia,* Berol. 1857: an abstract in Schmidt's *Jahrbb.* Bd. cxvii. p. 330.

Schulz, °*De idiosyncrasia haemorrhagica,* diss. inaug. Berol. 1844.

Schünemann, *Arch. f. path. Anat.* Bd. xli. p. 287: also in Schmidt's *Jahrbb.* Bd. cxxxix. p. 172.

Spahn, °Diss. inaug. Giessen, 1867: an abstract in Schmidt's *Jahrbb.* Bd. cxxxix, p. 173. Three cases are reported, but only two appear to belong to hæmophilia.

Steiner, °*De haemophilia,* Diss. inaug. Berol. 1842.

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